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Original Communications

THE POSTOPERATIVE RECOGNITION AND FURTHER MANAGEMENT OF UNSUSPECTED CERVICAL CARCINOMA*

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A NEW clinical problem has arisen. This is the recognition of unsuspected cervical carcinoma after hysterectomy has been done for myoma or prolapse. This problem formerly occurred after vaginal hysterectomy or amputation of the cervix, but now is increasing with the greater performance of total hysterectomy. Tables I and II show the trend in hysterectomy at The New York Hospital during the past ten years. It seems that with the increased use of total hysterectomy, carcinoma of the cervical stump will gradually become less frequent and be replaced by a new entity—unsuspected cervical cancer which is first diagnosed in the laboratory after hysterectomy has been done for some other reason. Table III condenses the experience of the last ten years into two equal five-year periods.

This is not an attempt to study planned hysterectomy as a treatment for cervical cancer. Nor are any patients included in whom there was preoperative diagnosis or even suspicion of cervical cancer. In essence, we are considering early, asymptomatic carcinomas which were not recognized clinically, but which are first diagnosed after hysterectomy has been done.

TABLE I.   TREND IN HYSTERECTOMY AT THE NEW YORK HOSPITAL, 1942-1946

YEAR	HYSTERECTOMIES SUBTOTAL	HYSTERECTOMIES TOTAL	NUMBER OF CERVICAL CANCERS DISCOVERED POSTOPERATIVELY	NUMBER OF NEW CERVICAL CANCERS
1942	223	33	0	31
1943	231	55	0	38
1944	249	50	0	30
1945	216	99	0	26
1946	247	128	0	33
Total	1.166	365	0	158

*Presented at a meeting of the New York Obstetrical Society, Nov. 13, 1951.

TABLE II. TREND IN HYSTERECTOMY AT THE NEW YORK HOSPITAL, 1947-1951

YEAR	HYSTERECTOMIES		NUMBER OF CERVICAL CANCERS DISCOVERED POSTOPERA- TIVELY	PER CENT HYSTEREC- TOMY	NUMBER NEW CERVICAL CANCERS	PER CENT DISCOVERED POSTOPERA- TIVELY
	SUBTOTAL	TOTAL				
1947	126	293	2	0.7	33	6
1948	47	383	9	2.3	66	9
1949	32	404	3	0.8	47	3
1950	23	440	1	0.3	38	1
1951	27	356	6	1.6	43	6
Total	255	1,876	21	1.1	227	10

TABLE III. EXPERIENCE OF LAST TEN YEARS CONDENSED INTO TWO EQUAL FIVE-YEAR PERIODS

YEARS	1942-1946	1947-1951
Hysterectomies.—		
Subtotal	1,166	255
Total	365	1,876
Number cases of cervical cancer discovered after hysterectomy.—		
Stage 0	0	9
Stage I	0	12
Per cent hysterectomies unsuspected cancer	0	1.1
Number cases of new cancer.—		
Stage 0	0	37
Stage I	158	190
Per cent cases of new cancer discovered after hysterectomy.—		
Stage 0	0	25
Stage I	0	6

TABLE IV. CLINICAL DATA ON 21 PATIENTS WITH UNSUSPECTED CERVICAL CANCER

	SQUAMOUS		ADENOCARCINOMA
	STAGE 0	STAGE I	
Total Number	9	10	2
Symptoms suggestive of cancer.—			
Yes	2	3	0
No	7	7	2
Cervix.—			
Normal	6	5	1
Erosion	3	5	1
Preoperative diagnosis.—			
Myoma	5	9	2
Prolapse	3	1	0
Ovarian cyst	1	0	0
Preoperative smears or biopsies.—			
Yes	1	0	1
No	8	10	1
Operation.—			
Total hysterectomy	3	2	0
Total hysterectomy and unilat- eral salpingo-oophorectomy	1	4	0
Total hysterectomy and bilat- eral salpingo-oophorectomy	2	2	2
Amputation of cervix	1	0	0
Vaginal hysterectomy	2	2	0
Postoperative treatment.—			
None	9	5	0
Surgery	0	0	0
Irradiation	0	5	2

Clinical Data

Twenty-one patients were discovered to have unsuspected carcinoma of the cervix during the past five years at The New York Hospital. For brevity, the data regarding these patients are presented in Table IV.

Comment

A. Diagnosis.—

Unsuspected carcinoma of the cervix was detected in about 1 per cent of the hysterectomies done at The New York Hospital. Johnson[3] reported the postoperative discovery of three cervical cancers in 300 colporrhaphies. Diddle and Bennett[2] found that seventeen of the 992 cervical cancers which were treated in Dallas from 1943 to 1946 were diagnosed after total hysterectomy had been done. Speert[5] found that fourteen, or 2 per cent, of the cervical cancers which were treated at the Roosevelt Hospital over a 20-year period were diagnosed postoperatively. Schmidt[4] included eighteen inadvertent hysterectomies in a study of the effect of hysterectomy on early cervical cancer.

From the viewpoint of the total number of cancers, 25 per cent of the Stage 0 cancers and 6 per cent of the Stage I cancers were detected postoperatively. Most of these cancers were asymptomatic or without physical sign. Five of these 21 patients, 25 per cent, deserved further preoperative work-up. Two of these patients had Stage 0 cancer; one of these with prolapse had noted bleeding which was attributed to a pessary, the other had a lesion just inside the external os which bled on contact. Three of these patients had Stage I cancer. Two had cervical erosions which bled on contact, while the third had noted postmenopausal bleeding for the past six months. These five patients would have benefited by additional preliminary diagnostic tests.

What preliminary tests are indicated when there are no symptoms or signs of cervical cancer? Routine smears and biopsies were not obtained because of the time and expense. Table V lists the various procedures which might have helped in preoperative diagnosis. Since about half of these cancers were at the squamocolumnar junction and the other half were up the endocervical canal, the minimum of diagnostic tests would include: (1) multiple cervical biopsies at the squamocolumnar junction, and (2) endocervical curettage or smears. All these procedures can be readily done without anesthesia. Sometimes, however, even repeated cervical biopsies will not detect the cancer, and it will be found only when the entire cervix is available for sectioning.

TABLE V.   PREOPERATIVE DIAGNOSTIC TESTS

Smears.—
    Vaginal
    Cervical Contact
    Endocervical
Biopsy.—
    Multiple Punch
    Ring
    Wedge
Curettage.—
    Endocervix

The types and locations of cervical cancer which are most likely to be diagnosed postoperatively are outlined in Table VI. An old gynecological dictum states that carcinoma is never associated with prolapse. However, there were five instances of this association in this small series. Certainly, the mere

descent of the uterus should not deter us from being suspicious of cancer and from taking smears and biopsies. Ashton[1] in 1947 reported two carcinomas of the cervix associated with prolapse among the 274 cervical cancers seen at the Woman's Medical College Hospital of Philadelphia from 1931 to 1946. She also collected 78 such combined lesions reported up to 1943.

B. *Pathology.*—

None of the cancers were recognized clinically either on admission or when the patient was examined under anesthesia just prior to surgery. Nor were they recognized when the cervix was sectioned. Carcinoma was diagnosed for the first time when the stained sections were examined microscopically. This was due partly to the early stage of the cancer and partly to the location of the cancers, as shown in Table VII. The absence of symptoms and the normal external appearance of the cervix in the majority of cases led to the primary diagnosis of myoma or descensus without consideration of the possibility of a coexisting carcinoma of the cervix. Similarly, the small size of the cancers coinciding with the earlier stages of cervical cancer caused failure in diagnosis.

TABLE VI. LOCATION IN WHICH CERVICAL CANCER IS MORE DIFFICULT TO DIAGNOSE

Cancer of endocervix
Cancer at squamocolumnar junction
Early cancer of exocervix
Cancer coexisting with prolapse

TABLE VII. LOCATION OF CANCER BY HISTOLOGICAL TYPE

	SQUAMOUS		ADENO-CARCINOMA	TOTAL
	STAGE 0	STAGE I		
Endocervix	2	5	2	9
Squamocolumnar junction	7	3	0	10
Exocervix	0	2	0	2

The 21 cancers in this report represent the residuum after review by several pathologists. All disputed diagnoses were rejected. Nine of these cancers were Stage 0. Whether these early lesions be called carcinoma in situ or intraepithelial cancer or noninvasive cancer, suffice it to say that the nine cervices which were classed as having Stage 0 cancer showed localized anaplasia which was histologically identical with the cellular changes of invasive cancer. Ten of the cervices showed Stage I cancer. All of these were confined to the cervix except one, which showed beginning spread to the paracervical tissue. Although the World Health Organization staging of cervical cancer is based solely on clinical evidence, these stages have been modified in this report to represent the actual extent of the cancer as determined by the available histological evidence. Hence Stage 0 was early, confined, noninvasive cancer as shown by repeated histological sections, while Stage I was cancer which was proved by repeated examination to be invasive, but still restricted to the cervix. However, since only the uterus was available for study, some of these Stage I cancers might belong to higher stages. No histological staging was done until repeated sections of the cervix had been examined. This inspection of many sections was invaluable, since one or two sections might show no carcinoma or a lower stage, while several sections permit the pathologist to be reasonably sure of the histological staging. Frequently new sections were made or sections were put lower in the block of suspicious sections.

Fig. 1 (Case 1).—Longitudinal section showing squamous cancer at squamocolumnar junction. Note normal appearance of exocervix. (×7.)
Fig. 2 (Case 1).—Cancer at squamocolumnar junction. (×300.)
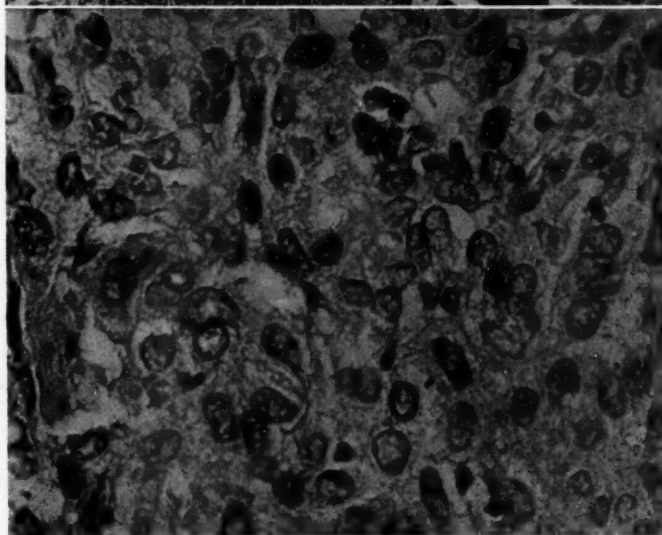Fig. 3 (Case 1).—Detail of area just inside external os. (×600.)

Fig. 1.

Fig. 2.

Fig. 3.

(For legends, see opposite page.)

TABLE VIII. PHYSICAL FACTORS IN IRRADIATION

	ABDOMINAL	VAGINAL
Kilovolts	250	100-140
Milliamperes	15	5
Skin target distance (cm.)	70	34
Half-value layer (mm.cu)	2.6	1.4
Port size (cm.)	15 × 10	3.6 × 9 plastic cone

C. *Treatment.*—

Preoperative recognition of cervical cancer would obviate the need for improvising treatment for carcinoma of the cervix discovered after simple total hysterectomy had been done. Our plan of treatment is in flux. The present formulation is as follows: The need for further treatment is determined by two factors: (1) the pathological stage of the cancer and (2) the completeness of the operation. If the cancer is Stage 0, additional sections of the cervix are studied to be sure that there is no invasion. If no invasive cancer is found, no further diagnostic tests or treatment are done, but the patient is subsequently examined at frequent intervals. This is in accord with the general feeling that simple total hysterectomy is adequate treatment for Stage 0 cancer. If the cancer is shown to be invasive, but apparently confined to the cervix, i.e., Stage I, bowel and bladder are studied by endoscopy and x-ray. After these preliminary diagnostic tests, x-ray irradiation is administered to most patients. The completeness of the preceding operation also influences further treatment. If only cervical amputation has been done, hysterectomy or irradiation, or both, are considered. If, as in the more common situation, one tube and ovary, or both tubes and ovaries, remain, no attempts have been made to remove these, since metastasis from cervical cancer to the tube and ovary is so rare. Lymph node dissections have not been employed, but might be attempted in the future. However, x-ray irradiation has been given by abdominal ports and occasionally by vaginal ports.

Our philosophy of treatment is this—the cancer may have been completely removed by hysterectomy but, nevertheless, we should give the patient every additional safeguard, which at the present time means irradiation. None of the patients with Stage 0 cancer have had further treatment, but half of the patients with Stage I cancer and both of the patients with adenocarcinoma have received irradiation therapy. In retrospect it would appear that all of the patients with Stage I cancer deserved x-ray irradiation. This is especially true when we consider the mounting evidence that 20 per cent of all so-called Stage I cancers of the cervix are false Stage I cancers and actually have spread beyond the cervix.

The physical factors of the customary x-ray irradiation are outlined in Table VIII. We have striven to administer a dose of approximately 4,000 to 5,000 r at point B in the parametrium 5 cm. lateral to the midline. The details of the patients who were treated are summarized in Table IX.

Several problems arose during irradiation therapy. One was how soon after operation could x-ray be started. Some radiologists have reported severe irradiation reactions in the immediate postoperative period. However, our experience with irradiation of patients after hysterectomy had been done for endometrial cancer suggested that treatment could be started 10 to 20 days after operation without marked ill effects. So we have followed that general plan with the reservation that irradiation may be stopped temporarily if a

Fig. 4 (Case 2).—Longitudinal section showing squamous cancer of endocervical glands. The vaginal portion of the cervix and the fornix are normal. (×7.)

Fig. 5 (Case 2).—Invasion of glands of endocervix. (×300.)

Fig. 6 (Case 2).—Cancer in endocervical gland. (×600.)
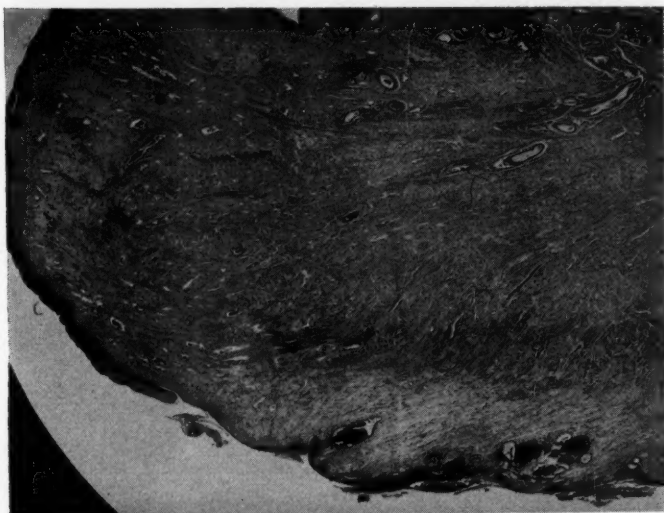
Fig. 4.

Fig. 5.
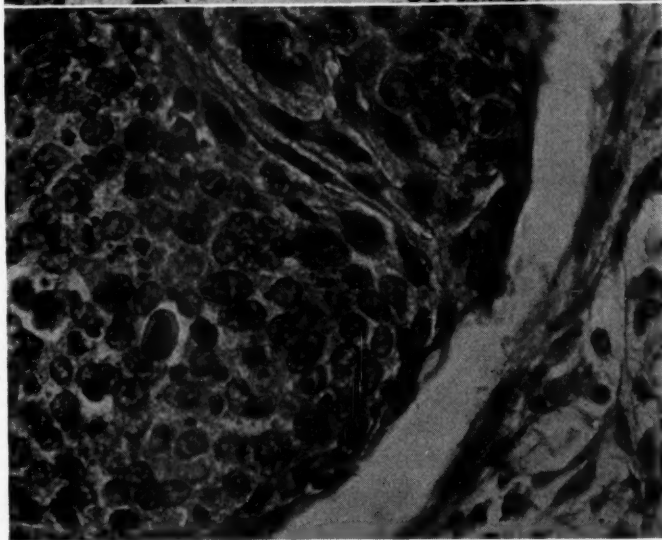
Fig. 6.

(For legends, see opposite page.)

TABLE IX. DATA ON PATIENTS TREATED BY X-RAY IRRADIATION

OPERATION	STAGE AND TYPE	INTERVAL IN DAYS FROM OPERATION TO IRRADIATION	DURATION IN DAYS OF IRRADIATION	PORTS, NUMBER AND LOCATION	DOSE PER PORT IN ROENTGENS	PARAMETRIAL DOSE IN ROENTGENS
1. Vaginal hysterectomy	Squamous I	20	28	6 Abdominal	2,150	4,100
2. Total hysterectomy, unilateral salpingo-oophorectomy	Squamous I	56	15 27	6 Abdominal	2,200	4,600
3. Total hysterectomy	Squamous I	15	38	6 Abdominal 3 Vaginal	1,600 3,000	4,850
4. Total hysterectomy, unilateral salpingo-oophorectomy	Squamous I	23	48	6 Abdominal 1 Vaginal	2,250 5,250	3,500
5. Total hysterectomy, bilateral salpingo-oophorectomy	Adenocarcinoma I	10	54	6 Abdominal	2,200	3,800
6. Total hysterectmy, bilateral salpingo-oophorectomy	Adenocarcinoma I	14	14	1 Vaginal	6,000	• 0
7. Total hysterectomy, unilateral salpingo-oophorectomy	Squamous I	Still receiving treatment				
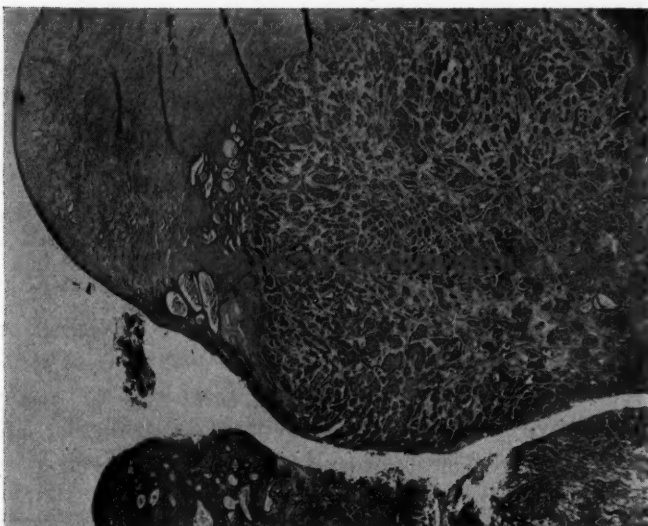
Fig. 7.
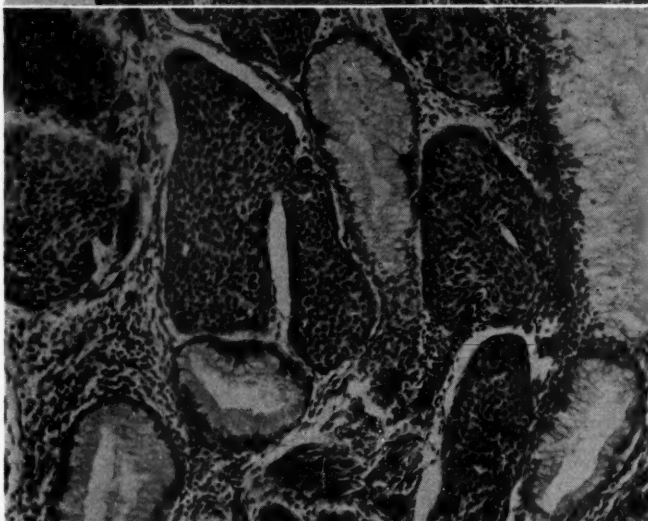
Fig. 8.
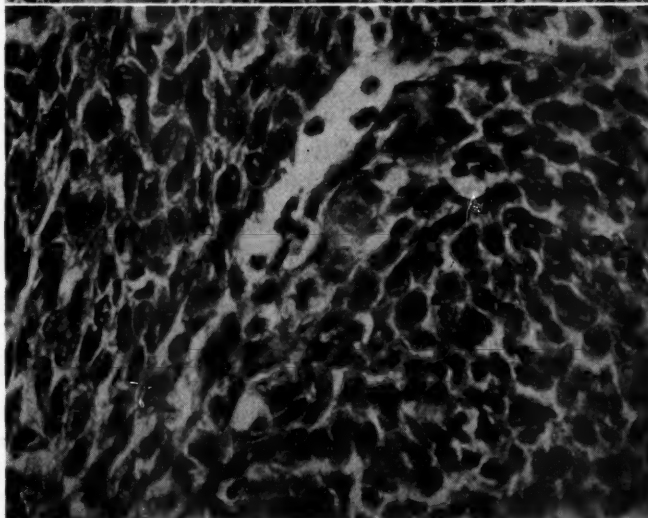
Fig. 9.

Fig. 7 (Case 3).—Extensive squamous cancer of endocervix covered by hollow shell of normal-appearing exocervix. (×7.)

Fig. 8 (Case 3).—Invasion of many endocervical glands by squamous cancer. (×300.)

Fig. 9 (Case 3).—Detail of endocervical gland completely filled by squamous cancer. (×600.)

serious reaction develops. One other problem was pain on insertion of vaginal applicators. So their use has been postponed until some time has elapsed after operation.

All patients are alive and without recurrences. Two have lived over four years, nine over three years, three more than two years, while seven are current patients.

Summary

Carcinoma of the cervix was discovered postoperatively in 21 patients during the past five years at The New York Hospital. Nineteen of these were squamous, 9 were Stage 0, and 10 were Stage I, while 2 were adenocarcinomas. The usual preoperative diagnosis was myoma or prolapse. Approximately 1 per cent of all hysterectomies resulted in undiagnosed cervical cancers. Sixteen were asymptomatic and had no physical signs, while five deserved further preliminary diagnosis, because of erosion, contact bleeding, or postmenopausal bleeding. Multiple biopsies of the squamocolumnar junction and curettage or aspiration smears of the endocervix would have resulted in preoperative diagnosis of the cancer. Nine of the cancers were in the endocervix, 10 at the squamocolumnar junction, while only 2 were on the exocervix. The cervical cancers which are mostly likely to be undiagnosed are (1) those of the endocervical canal, (2) squamocolumnar junction cancers, (3) very early cancers of the exocervix, and (4) cancer associated with descensus. None of the patients with Stage 0 cancer were treated further. One-half of the patients with Stage I cancer, and all of the patients with adenocarcinoma received irradiation. No additional surgery was done to remove tubes or ovaries. Problems in therapy consisted of (1) selection of the appropriate time to start treatment, and (2) postponement of the use of the vaginal cone during the immediate postoperative period. All patients are living and without evidence of recurrence. Fourteen patients have been observed for over two years, while seven are current patients.

Conclusions

1. The increased use of total hysterectomy is associated with an increase in the postoperative microscopic diagnosis of hitherto unsuspected cervical cancer. Conversely, carcinoma of the cervical stump is apparently declining.

2. These cancers are usually asymptomatic, are located in the endocervical canal or at the squamocolumnar junction, and are usually first diagnosed microscopically.

3. About 1 per cent of the total hysterectomies performed at The New York Hospital between 1947 and 1951 resulted in the detection of hitherto unsuspected cervical cancers. Twenty-five per cent of the Stage 0 cervical cancers, and 6 per cent of the Stage 1 cancers were so diagnosed.

4. Additional preoperative diagnostic tests were indicated in five of the patients, 25 per cent, because of cervical lesions or unusual bleeding. Multiple biopsies at the squamocolumnar junction and aspiration smears and/or curettage of the endocervix would have detected these cancers.

5. Stage 0 cervical cancer already treated by total hysterectomy requires only observation, while Stage I cancer apparently deserves abdominal x-ray irradiation.

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1. Ashton, D. L.: Am. J. Obst. & Gynec. 55: 299, 1947.
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3. Johnson, W. O.: Am. J. Obst. & Gynec. 56: 100, 1948.
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Discussion

DR. WILLIAM P. HEALY.—I might say it brings to my mind the question of how many cases I may have missed in the total hysterectomies that I have done, and yet I cannot recall a single instance, although I have a long period of years of follow-up of my private patients, in which cancer has appeared later in the pelvic lymph nodes in the cases in which I have done a total hysterectomy for a supposedly nonmalignant lesion. I have never had that experience, so it would seem to me that the total hysterectomy in Stage 0 and Stage I cases is probably good therapy in the vast majority of instances, even if you do subsequently find cancer histologically.

Therefore, what we have to consider is whether total hysterectomy is good therapy in the event of an unsuspected early carcinoma, and in general I think it is. I do not recommend it as the treatment for diagnosed cancer of the cervix, Stage I or II, or more advanced. I recommend radiation therapy as against surgery.

I am rather doubtful of the actual therapeutic value of postoperative roentgen therapy in these cases. I certainly would be inclined not to use it. I think you cannot get in an adequate amount of worth-while radiation, spraying it around. You have no spot to shoot at. You do not know that there is cancer any place in the patient's pelvis or in the lymph nodes and I think it is not good therapy. It is more likely to harm the patient, temporarily at any rate, than it is to help her. I personally would not be inclined to use postoperative roentgen irradiation in any of these unsuspected cases.

The primary surgical procedure has done a great deal more for the patient's future well-being than any subsequent radiation therapy.

DR. JAMES A. CORSCADEN.—I want to make a personal allusion, if I may, to Dr. Finn. He has written a great many articles which I have had pleasure in quoting. I have a couple of ideals or sagas which I follow, or at least I make the pretense. One of them is: Study without thought is futile. The accumulation of a lot of stuff without making something out of it gets one nowhere. Second, thought without study is vicious and that is the crime that most of us commit, the so-called general impression, which, as Dr. Adrian Lambert used to say, was ''blood brother to general debility.''

I would like to draw attention to the accuracy with which Dr. Finn has accumulated his material and the thoroughness with which he has put it together. This is de luxe material. I happen to know something about the common run of cases going into Kings County over in Brooklyn. They have been treated by incomplete surgery. They have had supravaginal hysterectomy for Stages I, II, and sometimes III. The number of terminal cases following incomplete operation has trebled in the last five years. This is the one lesson I would like to take out of Dr. Finn's article, the importance of making complete diagnosis before undertaking any type of therapy for these benign conditions, whether you want to call it a curettage or an examination under anesthetic, including a biopsy or any other term. I do not care how far one goes, but I am sure that the practice of putting the patient up on the table in the Trendelenburg position without thorough examination under anesthetic should be corrected. There is a present vogue of not examining the patient on the table.

DR. FRANK R. SMITH.—I would like only to reiterate what Dr. Healy said. I was glad to hear him say it because we have at Memorial Hospital felt prophylactic irradiation was not indicated by the fact that you have removed the uterus and found by accident a Stage I cancer, or have found what now we are forced to call a Stage 0, though I object to the term. I still think that the precancerous lesion offers no reason for giving prophylactic irradiation. It is a damaging weapon if it is given in adequate dosage.

It was not quite clear to me whether it was only the Stage I cases to which Dr. Finn gave postoperative irradiation. I think that was the case, that he did not give them to the Stage 0, so called.

I was interested in Dr. Corscaden's philosophy. I must say that in recent years, where Memorial was formerly a dumping ground, especially for general surgeons who did an inadequate operation, perhaps not doing a biopsy and then saying that nothing else but irradiation was to be done, and then sent them to Memorial, we have seen a decrease in the curve of these helpless, mishandled patients and we have seen an increase in the favorable patients whose diagnoses have been made by the pathfinder smear, perhaps leading to adequate biopsy, so that our over-all group is all the time becoming more favorable for either surgery or irradiation. I must agree with Dr. Healy that I still think irradiation is the method of choice for carcinoma of the cervix.

DR. LOUIS M. HELLMAN.—I would like to compliment Dr. Finn on drawing attention to what I have considered a very grave gynecological error, namely, the doing of gynecological surgery on patients in the carcinoma age in whom the cervix has not been thoroughly examined. At the Kings County Hospital we have had a rule that no patient, however benign the cervix may appear, undergoes hysterectomy without both smear and biopsy having been performed on that patient.

About a month ago we made an error which I think is understandable but which I would like to report to you in some detail. This patient was admitted for treatment of a fibromyoma at the age of forty. She had a polyp of the cervix and the house officer in performing the routine cervical biopsy merely removed the polyp thinking he had done a biopsy of the cervix. The polyp was reported as benign. Pathological examination of the specimen from the total hysterectomy revealed carcinoma of the cervix involving the endocervical canal.

If it is permissible, I would like to ask Dr. Masterson, who performed the subsequent surgery on this patient to discuss it. After he has described the surgical findings, I think you can well understand that radiation could not possibly affect the lesion which we found in the cervix. Is it possible for Dr. Masterson to discuss this?

DR. JOHN G. MASTERSON.—The patient whom Dr. Hellman has described was submitted to a total hysterectomy and bilateral salpingo-oophorectomy the latter part of August. Pathological examination revealed a carcinoma of the cervix involving the endocervix and extending throughout the major part of the cervix. Postoperatively a course of deep x-ray therapy was begun. During the course of the x-ray therapy she was followed with smears and weekly pelvic examinations. The smears remained positive and it was the impression on pelvic examinations that there might be recurrence although it was difficult to evaluate because of the usual postoperative fibrosis along with the radiation she was receiving. Inasmuch as the smear remained positive and the pelvic findings were equivocal, we decided to go ahead and explore this patient, which was done just last week. On entering the abdomen there were noted numerous adhesions between the small and large intestines which in turn were adherent to the floor of the pelvis, especially in the region of the vaginal vault. At the top of the vaginal vault there was a firm mass that extended up into the left parametria and also involved the rectum and the lower sigmoid. We biopsied this mass in several places and obtained a frozen section report of epidermoid carcinoma. Inasmuch as the extension involved the rectum and the bladder, which had been brought over the vaginal vault in the usual manner for peritonizing the pelvis, we felt the patient's only chance of survival would be a radical pelvic

dissection. We therefore proceeded to remove the bladder, the entire vagina, the rectum, and lower sigmoid, followed by a bilateral pelvic node dissection. The ureters were implanted into a midline colostomy. To date, the patient has done well. It is remarkable that in this particular case only ten weeks had elapsed from the initial surgery and yet there had been apparently such extension under active radiotherapy. She had received perhaps two-thirds of her course by the time the operation had been performed. Interestingly enough, at the time of operation, although we did perform a node dissection, none of the nodes appeared to contain any carcinoma.

DR. FINN (Closing).—I believe that the discussers brought out the variance of opinion about the diagnosis and treatment of early cancer of the cervix. I would like to state once again this is not an attempt to recommend simple total hysterectomy as a treatment for cancer of the cervix.

Regarding postoperative irradiation, there is wide variation of opinion. Our feeling has been this: we have diagnosed the cancer only in the laboratory and we know that increasing evidence shows that approximately 20 per cent of the patients with Stage I squamous cancer are false Stage I. In other words, the cancer has already spread further than the cervix. Because of that we thought irradiation might be helpful. It may well be that nothing can help these patients or it may be that more surgery should be done.

Dr. Corscaden also mentioned the need for complete diagnosis. I thoroughly agree with this and I would like to state that all of these patients were examined first in the clinic; second, on admission; third, under anesthesia, and at no time during this period was the suspicion of cancer raised. If I were to mention the ones in whom it was felt indicated to take biopsies or smears and who were subsequently found to have early cancers and then were treated in other fashions, there would be an additional several dozen patients. Only five of these patients had symptoms or signs suggestive of early cancer. The other 16 had no lesion and nothing to suggest further diagnostic tests.

None of the so-called Stage 0 patients were treated. All the patients who were treated were Stage I.

I think Dr. Hellman is to be commended that he takes cervical smears and biopsies on all patients prior to major operations.

The problem, as Dr. Javert has very concisely stated, is the time and the expense involved in routine smears and biopsies. We have all met the problem of obtaining negative smears and biopsies even in the presence of cancer. To detect these extremely early cancers the minimum diagnostic test should consist of adequate sampling of the squamo-columnar junction and curettage of the endocervix. The problem is really one of how much can be done routinely and still keep the program on a practical basis.

THE BILATERAL PARAVESICAL-SUPRAVESICAL APPROACH FOR EXTRAPERITONEAL CESAREAN SECTION*

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THERE has recently appeared a trend to substitute transperitoneal cesarean, fortified with sulfonamide and antibiotic therapy, for extraperitoneal cesarean section.[1-5] Since there are and probably always will be obstetricians incapable of performing extraperitoneal cesarean section, this substitution is undoubtedly justified in localities where no one able to perform the extraperitoneal procedure is available.

Rational use of sulfonamide and antibiotic therapy involves a delay for culture of the infecting organism, during which period inappropriate agents may have been employed, and before use of a specific drug can be instituted.[6] Even when apparently specific drugs are used the organism may prove drug resistant.[6-10] Suppression of one organism may encourage rapid growth of associated pathological bacteria or fungi.[6, 7, 11, 12, 13, 14] Aside from possible toxic and allergic reactions[14] these agents may also mask the symptoms and signs of abscess formation. The sulfonamides and antibiotics have not completely eliminated mortality resulting from infection. We cannot foresee at this time whether or not these deficiencies will be corrected in the future; but we do know that, prior to the use of sulfonamide and antibiotic drugs, extraperitoneal cesarean definitely provided a greater margin of safety for infected parturients with obstructed labor than transperitoneal cesarean, the peritoneal exclusion operation, or cesarean hysterectomy.[15-17]

Because of these facts we feel that dissemination of knowledge concerning the various techniques of extraperitoneal cesarean section is important, and that residents should be taught these techniques.

In a previous communication[18] we stated that there are only two fundamental approaches to the lower uterine segment in performing extraperitoneal cesarean section. These approaches are best designated as the unilateral paravesical approach (Latzko,[19] Norton,[20, 21] Irwin[22]) and the supravesical (Waters,[23] Ricci,[24, 25] Cartwright[26]). Both approaches have disadvantages as well as advantages and we have combined the two approaches in an effort to develop what we believe is an improved technique. This technique, performed with the bladder collapsed, consists essentially of a bilateral paravesical dissection with separation of the bladder from the lower uterine segment (retroversical dissection) followed by supravesical dissection of the bladder from the peritoneofascial flap. For convenience of terminology we

have called this a bilateral paravesical-supravesical approach[18] and have employed it in 62 of 91 extraperitoneal cesareans.

In the course of 52 extraperitoneal cesareans Stansfield and Drabble[27] of England also concluded that this is the most satisfactory technique.

Rationale

The reasons for developing this approach rest on the respective merits and hazards of the unilateral paravesical approach, the supravesical approach, upon the desirability of having the bladder empty during the entire dissection, and upon the advantages of entering the uterine cavity through a transverse cervical incision.

1. Merits and Hazards of the Unilateral Paravesical Approach.—The paravesical approach offers the quickest and simplest method of reaching the lower uterine segment and we believe this to be its only merit.

The presence of the ureter constitutes the principal hazard. It frequently occupies anomalous positions where it may be easily injured by the inexperienced operator. Since the unilateral paravesical approach seldom gives good exposure, danger of ureteral or peritoneal injury is especially great when dissection in one paravesical space must be extensive enough to permit delivery of the average or better than average-sized infant.

We have encountered cases where the bladder was attached to the uterus so far laterally in one paravesical space that a unilateral paravesical approach on the opposite side was necessary; or so far laterally in both paravesical spaces that a supravesical approach was necessary.

The unilateral paravesical approach usually permits only an oblique or at best a low vertical uterine incision, the disadvantages of which, as compared to the transverse cervical incision, are discussed later.

Finally, if one should encounter uncontrollable uterine hemorrhage, this dissection permits pressure on, or ligation of, only one hypogastric artery; and cesarean hysterectomy would be exceedingly awkward.

2. The Merits and Hazards of the Supravesical Approach.—The supravesical approach has the distinct advantage of providing exposure for a transverse cervical uterine incision. It also permits, in the event of uncontrollable bleeding, temporary or permanent occlusion of both hypogastric arteries, and would readily permit cesarean hysterectomy.

Its primary disadvantage lies in that it attacks initially the supravesical area where peritoneum and bladder are most frequently and most extensively adherent. We have found this area much simpler to dissect when the bladder and attached peritoneofascial fold have been completely freed from the lower uterine segment, thus permitting better mobilization and exposure of these tissues. Furthermore, this approach does not obviate injury to the ureter, and injury to the bladder is more frequent than with the paravesical approach.

In June, 1950, Fortin[28] encountered an anomalous "powder-horn" bladder and urachus which was patent to within 3 cm. of the umbilicus; he had performed bilateral paravesical and retrovesical dissection which revealed the anomaly and was able to mobilize the abnormal bladder sufficiently to the left for a transverse cervical incision. This anomaly would preclude use of the supravesical approach alone and did prevent completion of the bilateral paravesical-supravesical approach which he usually employs.

One of us (G. A. B.) recently made two unsuccessful attempts to perform elective extraperitoneal cesarean. In the first case the primary operation had been an extraperitoneal cesarean of the bilateral paravesical-supravesical type, performed because of cephalopelvic disproportion and prolonged labor; and, as was our custom at that time, constant bladder drainage had not been instituted postoperatively. The patient voided spontaneously according to the hospital

records, but at the repeat operation the bladder was found, after both paravesical spaces had been cleared and retrovesical dissection completed, broadly adherent to the transversalis fascia at a point midway between the symphysis pubis and the umbilicus. This bladder could not be mobilized as in Fortin's case, and any supravesical dissection would have been both tedious and hazardous. Transperitoneal cesarean was accomplished without difficulty. We believe that this anomalous position of the bladder was due to its distention during the healing process after the primary extraperitoneal cesarean section. This experience has taught us the importance of constant postoperative bladder drainage for 36 to 48 hours.

In the second case, elective primary cesarean was indicated because of cephalopelvic disproportion in a secundigravida with a small android pelvis who had lost her first infant at six months' gestation because of premature separation of the placenta. Again, after both paravesical spaces and the retrovesical area had been cleared, a broad area of adherence between the bladder and serous peritoneum was found midway between symphysis and umbilicus. It would have been possible to separate these structures, but the importance of securing a good infant precluded taking the time to complete such an extensive supravesical dissection.

3. *Management of the Bladder.*—It is common practice to start both of these standard approaches to the lower uterine segment with the bladder partially distended with 150 to 250 c.c. of fluid.[19-23, 26] The bladder is then emptied for the major portion of the dissection. In our opinion the only advantage of a distended bladder is that it permits easy identification of the vesical veins which lie in the deeper portions of the perivesical fascia when performing the supravesical approach of Waters and Cartwright. Since we do not employ this plane of dissection in the deeper layers of the perivesical fascia except when necessary, and then usually toward the end of our dissection, a distended bladder offers no advantage. In its empty contracted state the bladder is a visible and palpable organ and the trabeculated muscle fibers of the vesical muscularis are readily recognized before injury to the mucosa occurs.

Furthermore, if the bladder is distended and cannot be emptied because of a displaced or plugged catheter, the distended organ interferes with exposure and is very easily injured. Performing this operation with the bladder empty obviates the possibility of an obstructed catheter after the bladder is distended, and also permits elimination of various irrigating equipment which is difficult to set up in some small hospitals.

Our present practice is personally to place a Malecot (wing tip) or Foley catheter in the bladder just before operation, to make certain that the bladder is empty, and to maintain constant drainage for two days postoperatively.

4. *Advantages of the Transverse Cervical Incision.*—The transverse uterine incision originally introduced in 1882 by Kehrer[29] for transperitoneal cesarean section was modified by one of us (L. E. P.),[30] who has demonstrated that making the transverse incision in the cervix behind the bladder has certain advantages. They are: (1) the incision lies in the course of the majority of cervical fibers as is demonstrated when the incision is made by splitting the fibers with the fingers after a short transverse incision has been made by sharp dissection; (2) it is placed in the noncontractile portion of the uterus where healing is not interfered with by postpartum uterine contractions; and (3) the incidence of rupture during subsequent pregnancies is lower than with vertical incisions, rupture rarely occurring prior to labor and then usually being incomplete and without dangerous bleeding. Many authors (Phaneuf,[30-36] Browne,[37] Lawrence,[38, 39] Cosgrove and Norton,[15] Waters,[23] and Cosgrove[40]) have discussed the advantages of the transverse cervical incision.

The Bilateral Paravesical-Supravesical Approach for Extraperitoneal Cesarean Section

With the above points in mind we have developed the following technique:

1. Preparation for Operation.—With the patient anesthetized and in lithotomy position the vulva and vagina are prepared with suitable antiseptic solutions. The condition of the cervix and the presenting part is determined. A Malecot or Foley catheter is placed in the bladder, which is emptied, and the catheter is left in place. The abdomen is then prepared with suitable antiseptics and, with the patient horizontal (when spinal anesthesia is employed) or modified Trendelenburg position, sterile drapes are arranged.

2. The Abdominal Incision.—The abdominal wall may be opened with either a midline suprapubic or a Pfannenstiel incision (Fig. 1, *A*). Unless there is a previous midline incison to be excised we prefer the Pfannenstiel incision. The Pfannenstiel incision, which follows Länger's lines, heals well and is superior cosmetically; especially in obese patients it provides better exposure of the paravesical spaces, and thus far we have not encountered subcutaneous hematomas. Both incisions have the following advantages over the pararectus incision employed by some[20, 23] for extraperitoneal cesarean section: (1) they avoid the deep epigastric vessels; (2) they permit equal access to both sides of the pelvis; (3) they permit approximation of the rectus muscles when closing the abdomen; and (4) they may be complementary to the incisions of prior or subsequent gynecologic surgery.

The midline incision extends upward for 10 or 12 cm. from the symphysis pubis (Fig. 1, *A*). It is carried through the midline of the rectus sheath. The bellies of both rectus muscles, together with the pyramidalis muscles, which are present in about 80 per cent of patients, are dissected out and separated. At this point dissection of the paravesical spaces begins.

The Pfannenstiel incision (Fig. 1, *A*) follows Länger's lines for about 10 or 12 cm., its midpoint being about 2 cm. above the symphysis pubis. This curved transverse incision is carried through the rectus fascia and the aponeurotic or muscular portions of the external and internal oblique muscles. The abdominal muscles are separated from the posterior surface of the deep fascia by blunt dissection. The sagittal fascial partition between the rectus muscles is then divided by sharp dissection above (Fig. 1, *B*) and below. If not already separated, the bellies of the rectus muscles are separated by blunt dissection with the fingers (Fig. 1, *C*).

3. The Bilateral Paravesical Dissection.—By blunt finger dissection the endopelvic fascia covering the empty bladder is separated on both sides from the posterior surfaces of the abdominal musculature and pelvic wall until the yellow chicken fat in the paravesical spaces is encountered. If use of the peritoneal staining technique[41] is desired, the peritoneal fascial flap is stained at this point. With the bladder retracted medially by a finger, the endopelvic fascia and areolar tissues occupying the paravesical space are then frayed by blunt and sharp dissection (Fig. 2, *A*) until the glistening bluish layers of the periuterine fascia is exposed. One can usually identify the posterior transverse fold lying over the lower uterine segment. The same procedure is then repeated in the opposite paravesical space. An index finger is then inserted (Fig. 2, *B*) from one paravesical space to the other, between the easily separated perivesical and periuterine components of the endopelvic fascia (the retrovesical dissection). If a well-developed anterior transverse peritoneal fold presents at this point it may be divided from side to side by sharp dissection (Fig. 2, *C*), but this dissection is more often performed as the initial step of supravesical dis-

section. As the finger enters the opposite paravesical space it is usually necessary to divide one or more thin layers of endopelvic fascia overlying the finger tip (Fig. 3, *A*). This completes bilateral paravesical dissection and permits the bladder and attached peritoneofascial flap to be raised from the lower uterine segment.
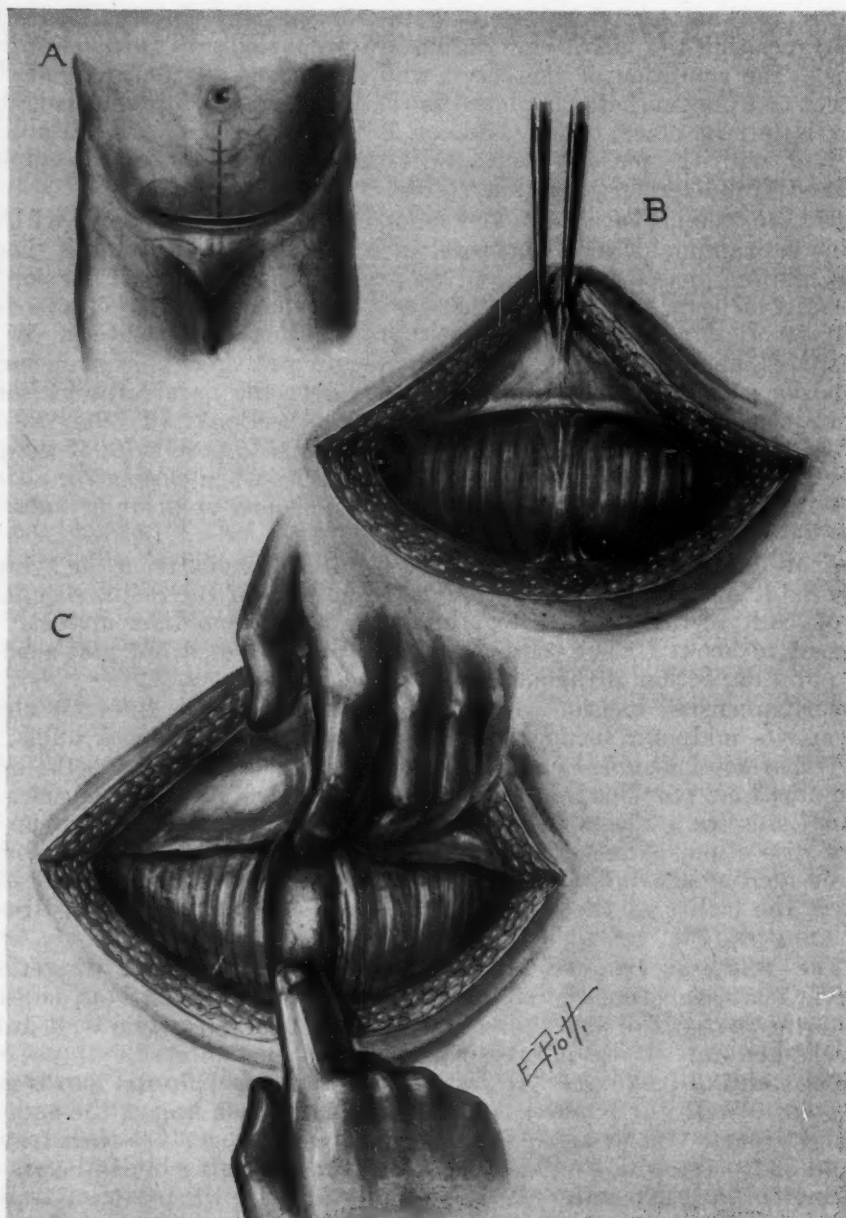
Fig. 1.—*A*, Illustrates the two types of incision which we employ for extraperitoneal cesarean section. The solid line represents the Pfannenstiel incision which we prefer. The dotted line represents the midline suprapubic incision which may be used.

B, Shows the Pfannenstiel incision carried to the abdominal musculature from which the upper flap of the deep fascia, grasped with Ochsner clamps, is raised. The sagittal fascial partition of this flap has been divided by sharp dissection. The sagittal fascial partition of the lower flap is likewise divided inferiorly to the symphysis pubis.

C, Illustrates separation of the rectus muscles with the index fingers, transversalis fascia appearing under the muscles.

Comment.—The paravesical dissection is carried out well down in the para-vesical space to avoid accidental injury to a low-lying vesicouterine peritoneal reflection. Dissection may reach the lower uterine segment laterally and in-
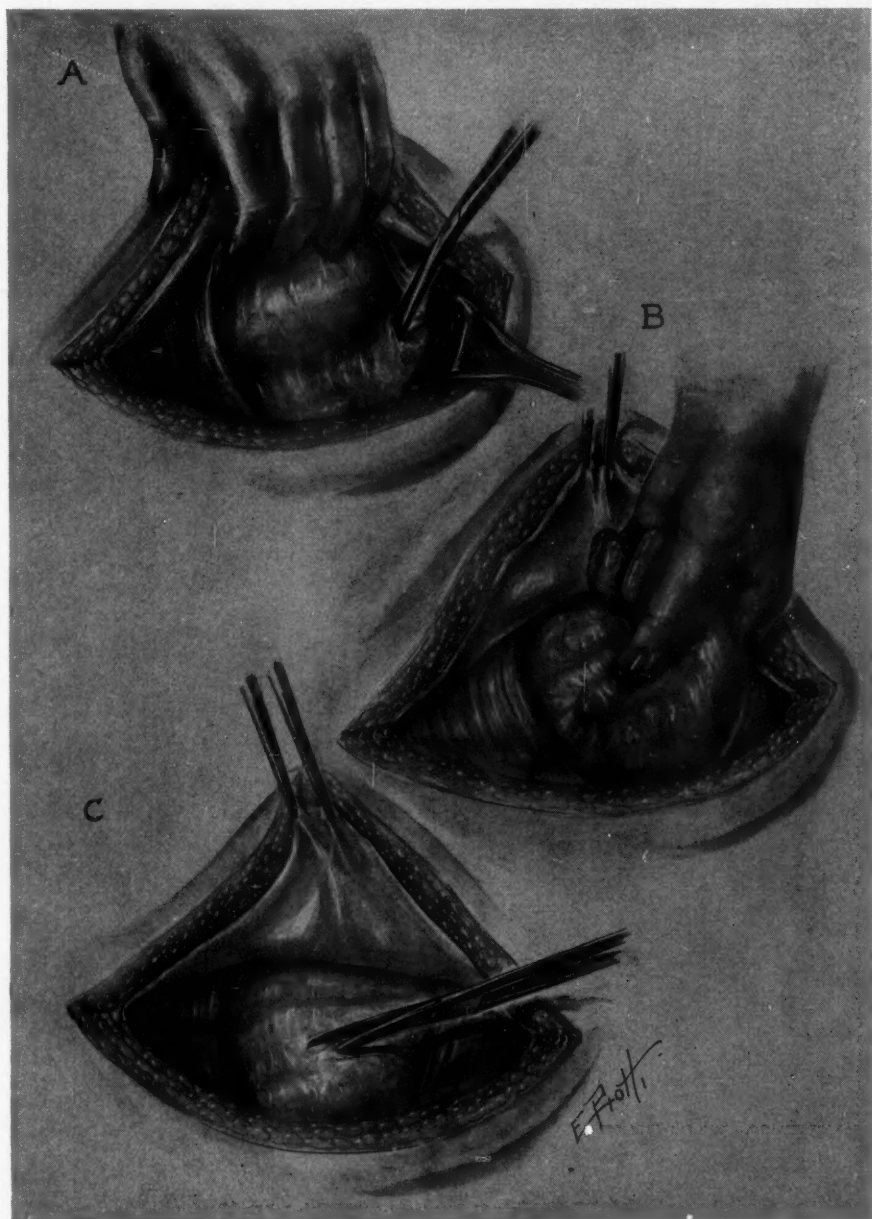
Fig. 2.—*A,* Illustrates one of the methods of performing paravesical dissection. The bladder lies mostly behind the symphysis pubis and in actual practice the dissection is performed beside the bladder at a point some distance inferiorly to that shown in the illustration.

B, Shows how the finger can be inserted retrovesically from one paravesical space to the other with the bladder in front, the uterus behind, and the peritoneofascial flap above. This loose areolar area is readily demonstrated when one forms the bladder flap in performing the Phaneuf cesarean, or panhysterectomy.

C, Demonstrates sharp dissection of a well-marked anterior transverse peritoneofascial fold. When such a fold is present, the dissection is usually done before the paravesical dissection but may be done afterward.

feriorly to the ureter. We have had this experience with one or both ureters in several cases, but in none have we injured the ureter. The only safeguard is recognition and isolation of the ureter before it is injured. The ureter usu-
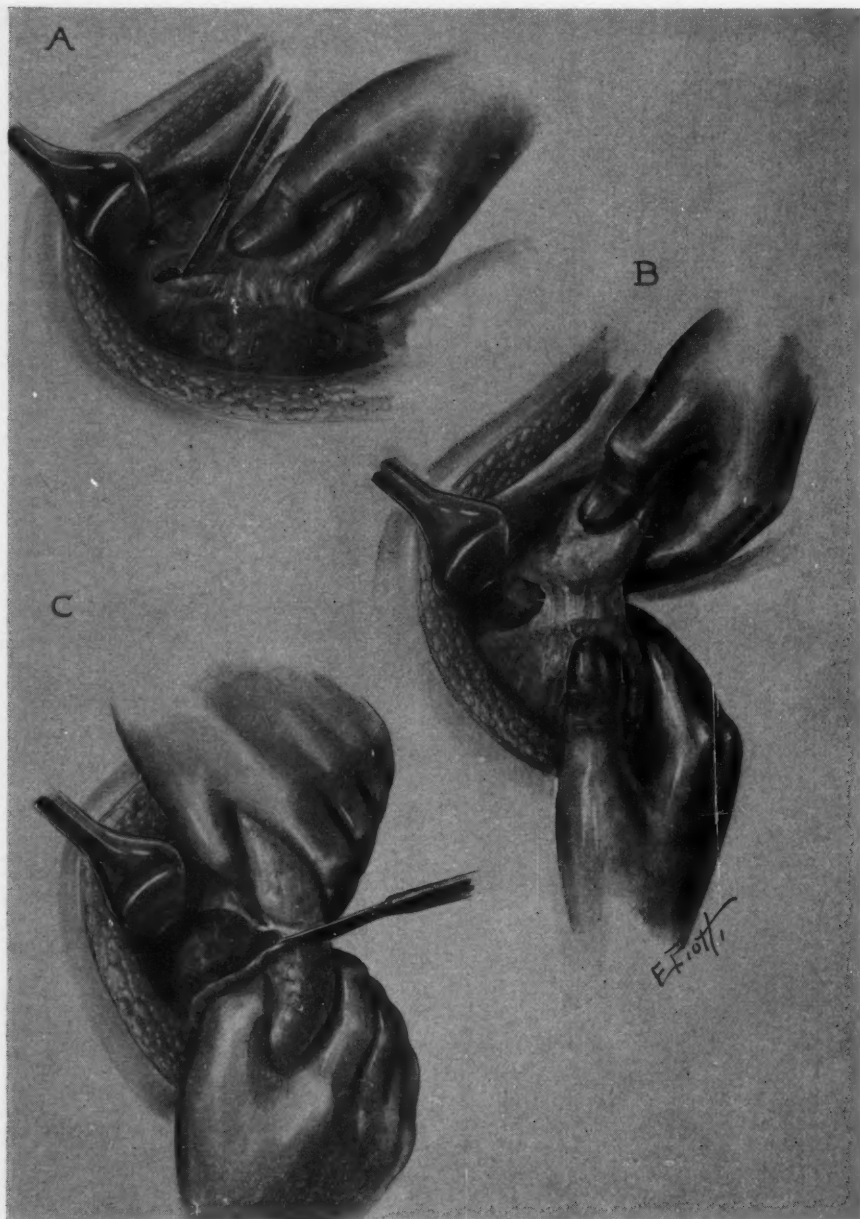
Fig. 3.—*A*, Illustrates completion of the paravesical and retrovesical dissection. By dividing the remaining tissue fibers of the right paravesical space over the tip of an index finger inserted through the left paravesical space and the retrovesical area, the bladder and attached supravesical area of peritoneofascial flap are freed from the lower uterine segment.

B, Shows the cleared right paravesical space, and the bladder and peritonefascial flap raised from the lower uterine segment. This illustration exhibits a fairly wide area of subserosal peritoneum between serous peritoneum and bladder.

C, Illustrates rotation of the bladder and attached peritoneofascial flap through approximately 180 degrees to expose the posterior transverse peritoneofascial fold for dissection. This figure also demonstrates sharp dissection in the vesical fascia because of marked adherence of serous peritoneum to the perivesical fascia.

ally courses laterally and upward from the bladder, but this is not an anatomical constant because we have encountered ureters whose course from the bladder was laterally and downward. The substance of the ureter is not constant but even late in pregnancy peristalsis can usually be elicited by me-
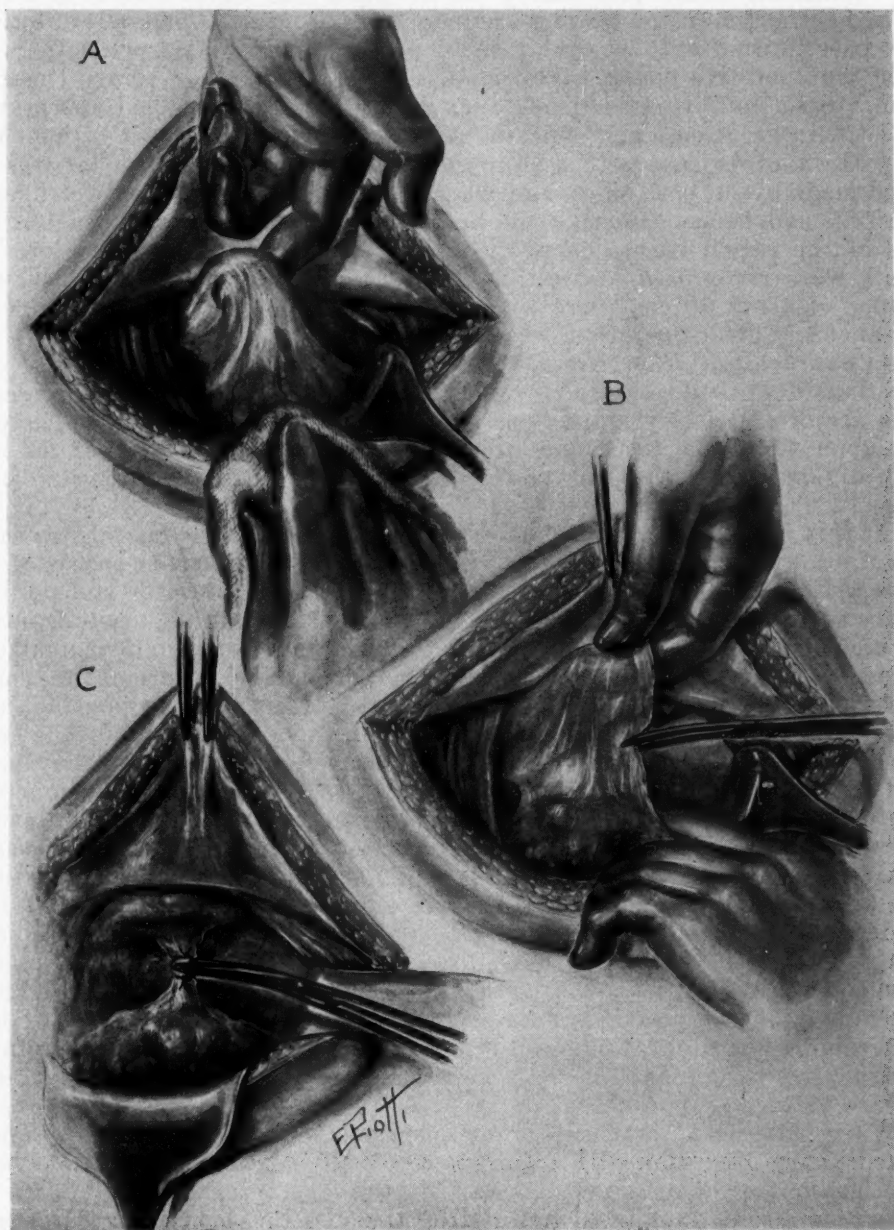
Fig. 4.—A, Illustrates a method of separating the bladder from the peritoneofascial flap by wiping the bladder down with a moist gauze sponge. This method is useful only in areas where serous peritoneum and perivesical fascia are not too adherent.

B, Demonstrates final dissection of fascial tissue between the bladder and the peritoneum toward the urachus. The artist has shown more subserous peritoneum than is commonly present.

C, Illustrates division of the urachus between two ligatures with final separation of the peritoneofascial flap above from the bladder below.

chanical stimulation. The structures most often confused with the ureter are the lateral umbilical ligaments (obliterated hypogastric arteries) which run from the internal inguinal ring to the umbilicus.

Paravesical dissection is most easily performed when a presenting head offers uniform and firm resistance to the fingers retracting the bladder medially. When the infant presents by the irregular and softer breech, identification and retraction of the bladder are more difficult. In the presence of a transverse presentation with irregular small parts or perhaps no presenting part under the operative site paravesical dissection immediately brings the great pelvic vessels into view. In one such instance the paravesical spaces were cleared with great ease and supravesical dissection accomplished without difficulty. In another case with a transverse lie the yellow chicken fat was displaced medially on both sides, and when bilateral paravesical and retrovesical dissection had been performed the ureters were discovered in the lateral aspects of the raised tissues connecting the peritoneum and the bladder. The ureters were recognized and although deprived of their blood supply for a distance of about 10 cm. there were no complications and the patient voided spontaneously after operation.

4. Supravesical Dissection.—Whereas dissection thus far is usually easy, dissection of the supravesical area where serous peritoneum and perivesical fascia are often densely and extensively adherent may be difficult. The principle upon which the technique offered rests is initial dissection of the most easily divided structures followed by final separation of remaining adherent areas.

At this point one has the bladder and attached peritoneofascial flap raised from the lower uterine segment (Fig. 3, *B*). This attachment consists of subserous peritoneum and endopelvic fascia making up the anterior and posterior transverse peritoneofascial folds. The anterior transverse peritoneofascial fold is demarcated laterally by the right and left lateral umbilical ligaments. Division of these ligaments permits better mobility and exposure of the remaining structures. Subsequent dissection is carried out as much as possible in the subserous peritoneum and the loose endopelvic fascia. Occasionally the entire anterior transverse peritoneofascial fold and transversalis fascia may be divided transversely throughout their entire width but more frequently adherence of serous peritoneum to perivesical fascia in the urachal area of the bladder makes division of only the two lateral portions of the fold advisable as an initial step. Division of the lateral accessible portions of the posterior transverse peritoneofascial fold results in even more mobility and exposure of the remaining undissected structures. Dissection up to this point is accomplished bluntly with the fingers or by sharp dissection between the bladder and serous peritoneum. By preference it is closer to the perivesical fascia than the serous peritoneum and the perivesical fascia is not violated if possible. If one loses the hernia-like peritoneal edge anteriorly the edge can be found by rotating the structures through 180 degrees and bringing the posterior peritoneofascial fold into view (Fig. 3, *C*).

When adherence between serous peritoneum and perivesical fascia is marked, sharp dissection with a knife is employed to isolate the peritoneum by dissecting in the outer layers of the perivesical fascia (Fig. 3, *C*). This dissection may also be facilitated by rotating the structures through 180 degrees. Sometimes the structures are easily separated by wiping the bladder off the peritoneofascial flap with a moist gauze sponge (Fig. 4, *A*). When there is considerable thin fascial tissue between peritoneum and bladder and no adherence between these structures, they can be rapidly separated by sharp dissection (Fig. 4, *B*); it is this type of anatomy which permits an occasional extraperitoneal cesarean to be performed with great ease and speed. Usually the last

structure divided is the urachus and if it gives any suggestion of being patent it is divided between ligatures of fine chromic gut (Fig. 4, *C*).

If the peritoneofascial flap thus isolated interferes with exposure of the uterus by virtue of a low attachment, the periuterine fascia just below the fold
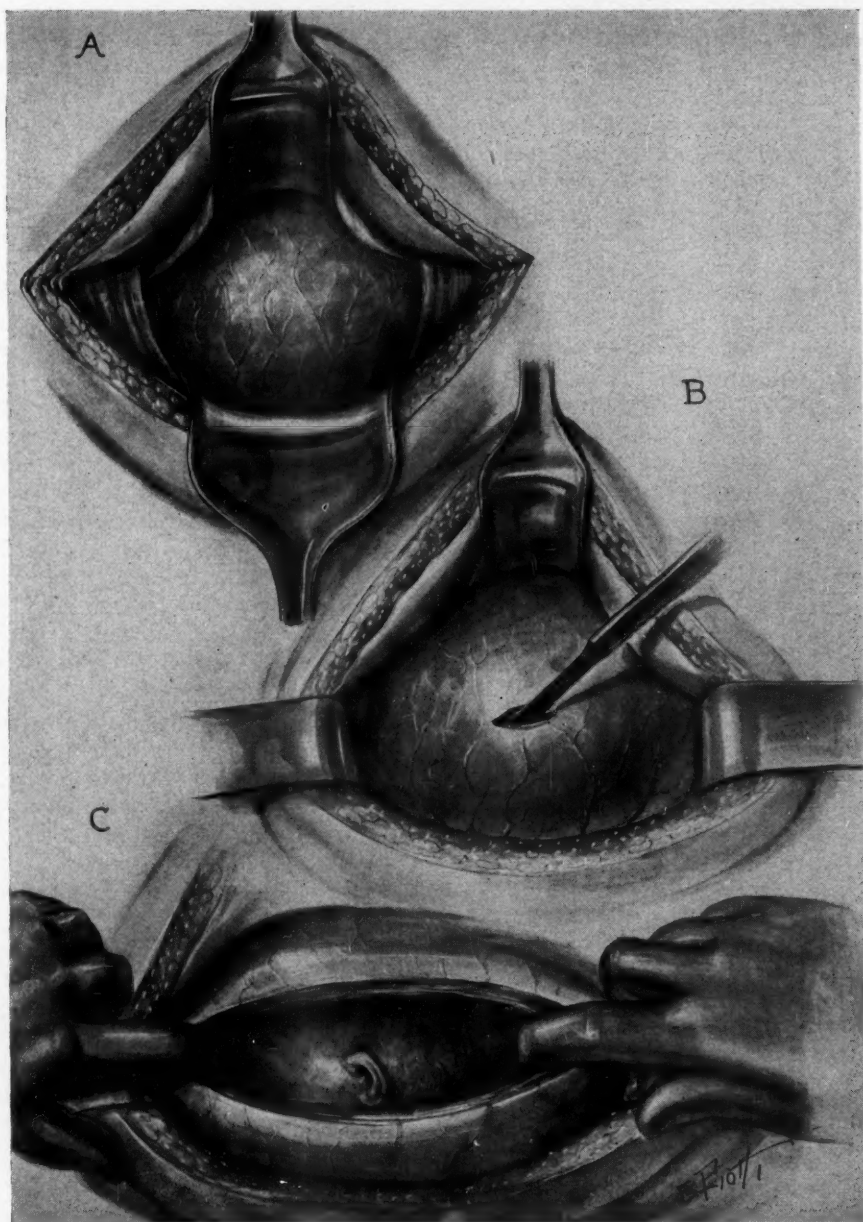
Fig. 5.—*A,* Demonstrates how the peritoneofascial flap is elevated with a Richardson retractor, and indicates the exposure of the lower uterine segment obtained. The empty bladder has been pushed down behind the symphysis pubis.

B, Illustrates the small transverse incision being made in the lower uterine segment by sharp dissection. When the presenting part is reached the index fingers are inserted into this incision.

C, Shows the method of extending the transverse cervical incision by splitting the tissues with the index fingers. A transverse incision made in this manner opens fewer vessels and results in less blood loss than an incision made by sharp dissection.

is scarified and by sharp and blunt dissection in the outer layers of peri-uterine fascia the fold is elevated to give the desired exposure (Fig. 5, *A*).

Comment.—We have previously mentioned the possibility of the ureters lying in the tissues whose dissection has just been described. Fortunately we have recognized these ureters and avoided injuring them. Bladder injury does occur from time to time but is infrequent. At no time, whether or not the bladder had been injured, have we had drainage of urine through the ab-dominal wall such as Ricci describes.[25] Accidental openings into the perito-neum are occluded by ligatures placed under a suitable clamp. We have pre-viously mentioned two cases where supravesical dissection was impossible be-cause of congenital or artificial anomalies.

5. Delivery of Infant and Closure of the Abdomen.—A transverse incision is made low on the uterus. This is usually performed by making a central transverse incision about one-half inch long (Fig. 5, *B*) and then enlarging the incision transversely with the index fingers (Fig. 5, *C*). If the incision thus made is not adequate the two extremities are carried upward with bandage scissors and thus far we have not encountered unusual bleeding. The infant is delivered manually or by vectis or by forceps according to the circum-stances. The umbilical cord is divided between clamps. If the placenta and membranes are not readily expressed we remove them manually. The uterine cavity is inspected for retained secundines which are removed if present. The patency of the cervical canal is ascertained by a finger or a blunt instrument. The uterine incision is repaired in two layers: (1) interrupted sutures of No. 0 chromic gut approximating myometrium to myometrium, excluding endometrium, and (2) a continuous Lembert or Cushing suture of No. 0 chromic gut infolding the uterine fascia over the first line of suture. The entire operative site is inspected, any bleeding is controlled and any visible remnants of vernix caseosa are removed. A split rubber tissue drain is placed so as to drain both paravesical spaces; it is brought out in the lowest point of the midline and anchored to the skin with an interrupted suture. The rec-tus muscles are loosely approximated with several interrupted sutures of No. 00 chromic gut. The lateral portions of the internal oblique muscles and aponeuroses are approximated with interrupted sutures of No. 00 chromic gut. The aponeuroses of the external oblique and the rectus sheath are approx-imated with interrupted sutures of No. 0 chromic gut. Scarpa's fascia is loosely approximated with a continuous suture of No. 000 plain gut. The skin edges are approximated with a continuous locked suture of fine Dermalon placed on either site of the drain.

If a longitudinal incision has been used the rectus muscles are approx-imated loosely with several interrupted sutures of No. 00 chromic gut, the rectus fascia is approximated with interrupted sutures of No. 0 chromic gut, Scarpa's fascia is approximated with a continuous suture of No. 000 plain gut, and the skin edges are approximated with a continuous locked suture of fine Dermalon. The contractile state of the uterus and the presence of vaginal drainage are ascertained.

Injuries to the Peritoneum

We have opened the peritoneum in 30 of these 91 operations. It is gen-erally felt that closure of such peritoneal injuries by ligature prior to opening the uterine cavity provides the patient with adequate protection against peri-tonitis. When the peritoneum is opened accidentally early in the course of dissection, and if inspection shows the area of adhesion of serous perito-neum to perivesical fascia to be extensive we proceed to circumcise this area of adhesion. This leaves an area of serous peritoneum on the bladder dome

and the large opening in the peritoneofascial flap is closed transversely with a series of overlapping ligatures. We have seen this method used for many years but do not believe it should be standard procedure as suggested by Cacciarelli.[42] We regard the record of Stansfield and Drabble[27] who opened the peritoneum in only two of fifty-two consecutive extraperitoneal cesarean sections as remarkable.

Injuries to the Bladder and Ureters

Bladder injuries when recognized and properly repaired do not result in undue complications. When bladder muscularis has been violated substantially, or when bladder mucosa is exposed, repair is accomplished by a continuous suture of fine chromic gut in the muscularis and fascia reinforced by a series of interrupted sutures of the same material. When the bladder cavity has been opened we have found the same two layers of suture to be adequate with the patient placed on constant bladder drainage for one week.

The possibility of bladder fistulas is a real one. We have repaired a combined uterovesico and cervicovaginal fistula following a Norton type cesarean section performed on a badly infected parturient in another state. Investigation showed that the bladder had been repaired with a single line of heavy chromic gut. We have had one instance (the initial error was a distended bladder due to a Nélaton catheter which became obstructed) where in performing paravesical dissection the vagina was opened and during retrovesical dissection a hole was made in the posterior aspect of the bladder just above the trigone. It was impossible to expose this injury for repair either before or after delivery of the infant. The bladder was opened anteriorly and the posterior defect closed with several interrupted sutures of fine chromic gut. When a Malecot catheter was removed at the end of seven days vaginal leakage of urine was noted. The Malecot catheter was replaced and the vesicovaginal fistula closed spontaneously on the seventeenth postoperative day. Both of these cases are being reported elsewhere.[43]

Control of Uterine Hemorrhage

While we have not experienced uncontrolled uterine hemorrhage in our own cases we do know of one case in another state where the patient lost her life because of operative hemorrhage from the uterus during a Waters type of extraperitoneal cesarean section. We have demonstrated to ourselves repeatedly that hemorrhage from the uterus at the time of cesarean section can be controlled by pressure on the hypogastric arteries just as such pressure (or ligation of the arteries) controls hemorrhage in gynecological patients. By making pressure on the hypogastric arteries we have experimentally produced a practically bloodless field for closure of the uterine incision. An alternative method of managing this situation would be opening the peritoneum and performing rapid cesarean hysterectomy. These two methods might of necessity be combined.

We feel it desirable to have both paravesical spaces cleared for pressure on the hypogastric arteries in the event of uncontrollable uterine hemorrhage.

Postoperative Care

Postoperative care of a patient who has had an extraperitoneal cesarean section is predicated largely by her condition before operation and the indications for operation.

While many people do not drain the operative site it is in our opinion that such a large area of cellular tissue should be routinely drained. The case

mentioned under the merits and hazards of the supravesical approach has persuaded us that, although over 80 per cent of patients will void spontaneously, maintenance of constant bladder drainage for 36 to 48 hours is important. We routinely use a full dosage of Gantrisin during constant bladder drainage and for 24 hours thereafter.

In the infected parturient we employ antibiotics as necessary. We also use blood transfusions as indicated. Any one of several types of sedation is used. We routinely give a course of Ergotrate following operation and if we suspect postpartum atony we dissolve two ampules of Ergotrate in 1,000 c.c. of normal saline or 5 per cent glucose and administer this intravenously over a period of several hours to maintain a contracted uterus. When the patients are not too exhausted from prolonged labor and are in relatively good condition we have them out of bed on the first postoperative day. The catheter is removed from the bladder the second postoperative day. If there is no evidence of infection we remove the rubber tissue drain on the third postoperative day. In the average case we remove the sutures on the ninth postoperative day and send the patient home on the tenth or twelfth day.

In these 91 operations there were no maternal deaths, and the circumstances of 4 infant deaths have been discussed previously.[44]

Summary

A technique for extraperitoneal cesarean section which has been employed in 62 of a series of 91 consecutive extraperitoneal operations is presented. This technique, for convenience, has been termed the bilateral paravesical-supravesical approach to the lower uterine segment. It results from an effort to combine the advantages of the unilateral paravesical approach and the supravesical approach, precluding their disadvantages as much as possible and permitting exposure for a transverse cervical uterine incision. We feel that extraperitoneal cesarean, properly performed by any of the standard techniques, is satisfactory, but that anatomical variations which may prevent consistent use of any single approach are most logically managed by the technique described. Dissection is performed with the bladder empty. The transverse cervical incision is employed.

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PREGNANCY ASSOCIATED WITH CONGENITAL ABNORMALITIES OF THE FEMALE REPRODUCTIVE TRACT

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CONGENITAL malformations of the female reproductive tract have always been a topic of considerable interest among obstetricians and gynecologists. Besides being mere anatomical curiosities, they may present unusual and difficult obstetrical problems when associated with pregnancy. In recent years, numerous isolated case reports and small groups of case records have appeared in the literature; while not of frequent occurrence, these abnormalities have become sufficiently important to demand the attention of every practicing obstetrician.

Several relatively large series of cases correlating one particular type of abnormality with pregnancy and labor have been reported. However, no single study has been made to correlate the effects of different types of congenital malformations of the reproductive tract on pregnancy and labor. It is with this thought in mind that the authors have attempted to present the various types of uterine and vaginal anomalies encountered in obstetric patients seen in the Sloane Hospital for Women during the period 1925 to 1949, inclusive, emphasizing the clinical significance of each type of malformation on the course of pregnancy, labor, and the puerperium.

While many classifications of incomplete fusion of the Müllerian ducts have been proposed and are in existence, no such single scheme is available for international classification purposes. However, from the clinical standpoint, the following one proposed by Jarcho,[7] with several additions, seems to us to be the most satisfactory. These are schematically represented in Fig. 1.

Group 1—Uterus didelphys.
Group 2—Uterus duplex bicornis bicollis, vagina simplex.
Group 3—Uterus duplex bicornis unicollis, vagina simplex.
Group 4—Uterus septus.
Group 5—Uterus subseptus.
Group 6.—Uterus arcuatus.
Group 7—Uterus unicornis.
Group 8—Septate vagina.
Group 9—Congenital stricture of the vagina.

It may be of interest to note that none of our patients presented the rare condition of a pregnancy occurring in a rudimentary horn (Group 7). According to Stander,[16] this is the most common of the various abnormalities.

For comparison with standard statistics we have taken the results of the pregnancies observed at the Sloane Hospital for Women for the ten-year period, 1933-1942.

Uterus simplex

Uterus didelphys   **Uterus duplex bicornis bicollis Vagina simplex**   **Uterus bicornis unicollis Vagina simplex**

Uterus septus   **Uterus subseptus**   **Uterus arcuatus**

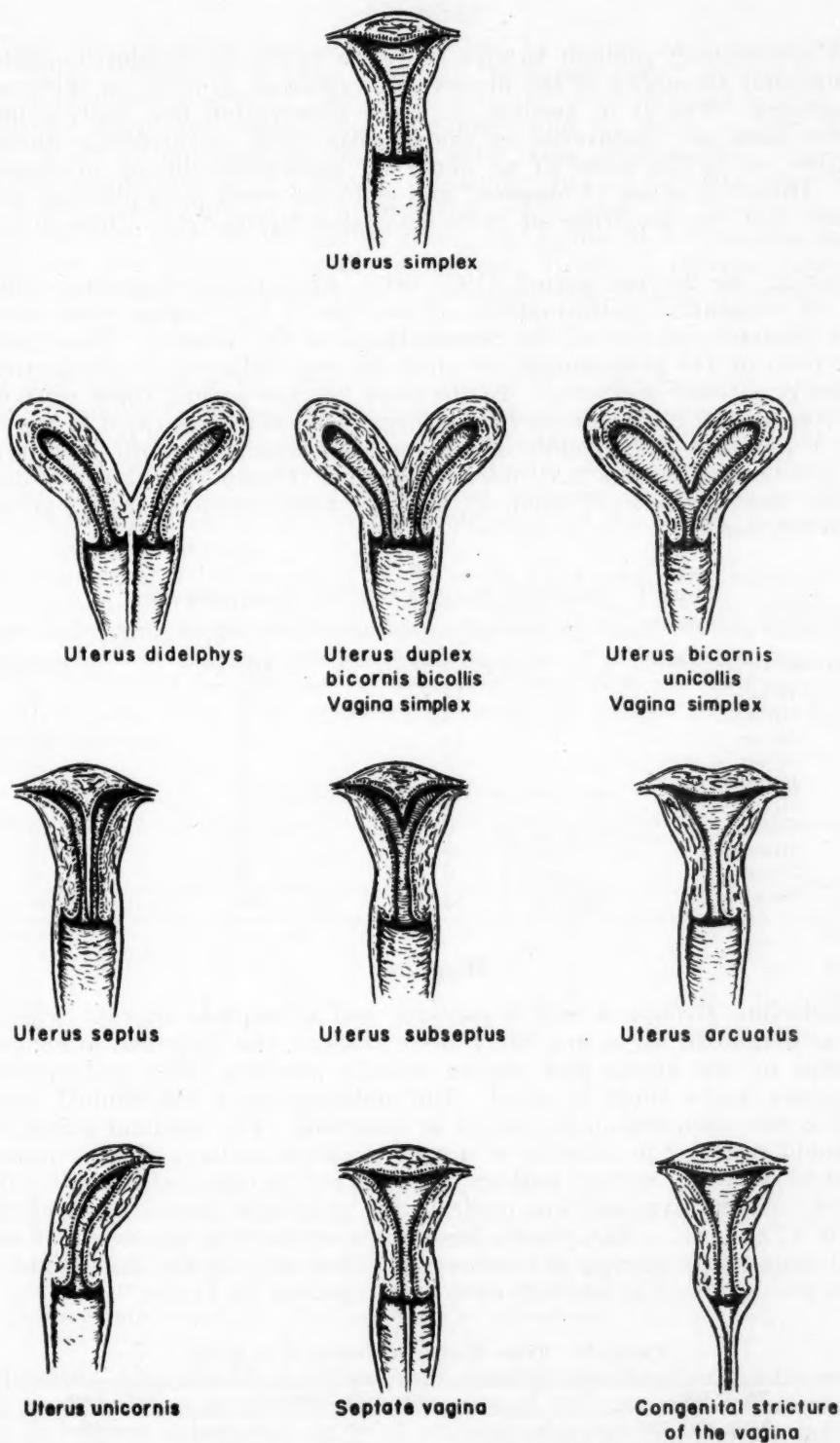**Uterus unicornis**   **Septate vagina**   **Congenital stricture of the vagina**

Fig. 1.—Congenital abnormalities of the female reproductive tract. (Reproduced in part from Jarcho, J.: Am. J. Surg. 71: 106, 1946.)

Incidence

It is extremely difficult to give a precise figure concerning the incidence of congenital anomalies of the uterus and vagina as so many of them remain undiagnosed. This is in keeping with the observation that quite a number of such cases are discovered at the autopsy table, accidentally during an operation, or in the event of an abnormal occurrence during pregnancy or labor. However, series of observed and collected cases from different sources indicate that the incidence of these anomalies varies from 0.004 to 3.8 per cent.[4, 8, 15]

During the 25-year period (1925-1949), 62 patients presenting different types of congenital malformations of the uterus and vagina were observed on the obstetric service of the Sloane Hospital for Women. These patients had a total of 146 pregnancies, of which 96 were followed in this institution, and the remainder elsewhere. In the same 25-year period, there were 60,788 deliveries, giving an incidence of 1 in every 633 deliveries (or 0.15 per cent). Table I presents the number of pregnancies associated with each type of abnormality, and reveals that uterus didelphys (Group 1) and uterus bicornis unicollis, vagina simplex (Group 3) were the most commonly found abnormalities in this series.

TABLE I.   INCIDENCE RELATED TO TYPE OF ABNORMALITY

TYPE OF ABNORMALITY	NO. OF PATIENTS	TOTAL NO. OF PREG.	
		AT SLOANE	ELSEWHERE
Group 1	18	29	9
Group 2	4	5	11
Group 3	14	25	12
Group 4	5	6	3
Group 5	3	5	11
Group 6	4	7	3
Group 7	0	0	0
Group 8	9	11	1
Group 9	5	8	0
Total	62	96	50

Diagnosis

Excluding Groups 4 and 5 (septate and subseptate uterus) where the physical diagnostic signs are likely to be obscure, the diagnosis of congenital anomalies of the uterus and vagina usually presents little problem, if the obstetrician keeps them in mind. Unfamiliarity with the clinical manifestations is the main reason for errors in diagnosis. The cardinal points which one should look for in arriving at a correct diagnosis have already been considered in detail by several authors and will not be repeated here.[5, 14] In our series, a correct diagnosis was made in the antenatal period in 44 of the 62 patients (Table II). The remainder were diagnosed in the event of an abnormal occurrence during the course of labor and in the immediate postpartum period. Similar findings have been reported by Taylor.[17]

TABLE II.   TIME WHEN DIAGNOSIS WAS MADE

DIAGNOSIS	NO. OF PATIENTS	PER CENT
Ante partum	44	70.9
Intra partum	8	13.0
Post partum	10	16.1
Total	62	100

Fertility

These abnormalities have been described by some[13] as favoring conception. Miller,[10] however, believes that any lesion associated with atresia and retention of placenta greatly lessens the fertility. Our data study only these aberrations when associated with pregnancy and we have no comparable control series of nonpregnant patients with these abnormalities; therefore, no valid conclusions can be drawn. However, the 62 patients presented a total of 146 pregnancies, or 2.3 pregnancies per patient. In view of the high cesarean section rate for the entire group, the figure of 2.3 pregnancies per patient does not appear markedly abnormal. Group 5 (uterus subseptus) appeared to be most prolific, with the 3 patients accounting for 16 pregnancies.

Abortion

It has been noted by different observers that patients with congenital uterine anomalies show a markedly increased tendency to abort, the incidence ranging from 24 to 53 per cent.[13, 17] The reasons advanced for the increased incidence are manifold. Abnormal implantation of the ovum, poorly vascularized uterine septa, fundic irregularities, malposition of the gravid horn, and, in some instances, marked underdevelopment of the uterus, have all been cited as etiological factors.

In this series of 146 pregnancies, 38, or 26.0 per cent, terminated as spontaneous abortions (Table III). Of these 38 abortions, 19 were observed in our institution and the remaining patients treated elsewhere. When these figures are interpreted in the light of the total number of pregnancies observed at the Sloane Hospital for Women, it becomes evident that the incidence of 19.7 per cent is more than three times as great as the Sloane Hospital abortion rate of 5.6 per cent.

TABLE III. INCIDENCE OF ABORTION

TYPE OF ABNORMALITY	TOTAL NO. OF PREG- NANCIES	NO. OF ABORTIONS			INCIDENCE %
		S.H.	ELSE- WHERE	TOTAL	
Group 1 (2 therapeutic)	38	6	5	11	28.9
Group 2	16	1	3	4	25.0
Group 3	37	6	7	13	35.1
Group 4 (1 therapeutic)	9	3	0	3	33.3
Group 5 (1 therapeutic)	16	3	3	6	37.5
Group 6	10	0	1	1	10.0
Group 7	0	0	0	0	0
Group 8	12	0	0	0	0
Group 9	8	0	0	0	0
Total	146	19	19	38	26.0

Corrected abortion rate, correcting for 4 therapeutic: 23.9 per cent.

Gross abortion rate at Sloane Hospital: 19.7 per cent, correcting for 4 therapeutic: 16.5 per cent.

Gross abortion rate elsewhere: 38.0 per cent, no corrections: 38.0 per cent.

However, 4 of the 19 abortions were carried out for therapeutic reasons, giving a corrected spontaneous abortion rate of 16.5 per cent. Patients with Group 5 (uterus subseptus) type of anomaly showed the highest incidence of abortion (37.5 per cent) with Groups 3 (uterus duplex), 4 (septate uterus), 1 (didelphys), and 2 (uterus duplex, double cervix) following closely in that order. Thirteen per cent, or 5 of these 38 abortions, were observed in the second trimester, and one of these was diagnosed as a molar degeneration.

Our study confirms the greatly increased abortion rate in these patients, although it is not quite as high as reported by other investigators.[13]

Term and Viable Births

If we accept 1,500 grams as the measure of viability and make the necessary corrections, only 97 pregnancies, or 66.4 per cent, resulted in viable births (Table IV). This is quite low when compared to the 93.1 per cent viable birth rate of Sloane Hospital; Smith[15] and Moncure[11] have also commented on this low viable birth rate.

If one further corrects for the prematures, then only 56.1 per cent of these deliveries actually went to term. This corresponds with the results obtained in the series reported by Miller.[10] (Normal term birth rate at the Sloane Hospital is 85.0 per cent.)

TABLE IV. VIABLE BIRTH RATE

Total number of pregnancies	146
Corrected for 38 abortions	108
Corrected for 9 infants under 1,500 grams	99
Corrected for 2 congenital abnormalities	97*
Giving 66.4 per cent viable births	
Compared to 93.1 per cent viable births at this Hospital	

*Includes 15 premature labors, but viable births.

Antepartum Complications (Table V)

1. *Hemorrhage.*—This was a complicating factor in 14 of the pregnancies. Six pregnancies, or 5.5 per cent (3 in Group 1, uterus duplex, double cervix, 2 in Group 3, uterus duplex, and 1 in Group 6, arcuate uterus), had premature separation of the placenta, which is quite high when compared to the 1.2 per cent occurrence of this complication at the Sloane Hospital. No placenta previa occurred in this series. In the remaining eight patients, all of whom had duplication of the uterus, the etiological factor was undetermined. Although this may have represented expulsion of a decidual cast from the nonpregnant horn, it is impossible from our data to confirm this viewpoint. However, the percentage of pregnancies with unexplained vaginal bleeding (7.4 per cent) was

TABLE V. ANTEPARTUM COMPLICATIONS

COMPLICATION	TYPE OF CONGENITAL ABNORMALITY									TOTAL
	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 6	GROUP 7	GROUP 8	GROUP 9	
1. Hemorrhage:										
a. Abruptio placentae	3	0	2	0	0	1	0	0	0	14
b. Placenta previa	0	0	0	0	0	0	0	0	0	
c. Cause undetermined	2	2	3	1	0	0	0	0	0	
2. Toxemia	2	1	0	2	2	3	0	1	1	12
3. Malpresentations:										
a. Breech	7	2	2	0	1	0	0	4	0	19
b. Transverse	1	0	1	0	0	1	0	0	0	
4. Premature rupture of the membranes	21	4	8	4	2	3	0	6	1	49
5. Hydramnios	0	0	0	0	0	0	0	1	0	1
6. Surgical complications	0	3	0	0	1	0	0	0	0	4
7. Medical complications	2	1	0	1	1	0	0	0	0	5
Total	38	13	16	8	7	8	0	12	2	104

decidedly greater than the 1.9 per cent recorded at the Sloane Hospital in all deliveries between 1933 and 1942.

2. *Toxemia.*—There were two patients who developed hyperemesis gravidarum. The condition was not severe enough to warrant a therapeutic termination of the pregnancy. Twelve patients had pre-eclampsia of varying degrees of severity in the last trimester of pregnancy. No patient in this series showed eclampsia. The general incidence of toxemia in this group was 11.1 per cent, which shows essentially no change from the hospital rate (14.2 per cent), as well as the usually quoted figure of 10 per cent in the general population. This is not in agreement with the findings of Miller[10] and Ernst[3] who have reported an increased incidence of toxemia in these patients. The uterus arcuatus (Group 6) contained the highest incidence of toxemia.

3. *Hydramnios.*—There was only one patient in Group 8 (septate vagina) who developed hydramnios, but she was delivered of a normal infant. This shows no change from the hospital incidence of hydramnios, 0.6 per cent.

4. *Malpresentation.*—There is a greatly increased frequency of breech and transverse presentations in patients with congenital uterine anomalies.[14, 15, 18] The speculative reasons advanced for this peculiar tendency are already too well known to merit any further description. In this series there were 16 breech and 3 transverse presentations, giving an incidence of 17.5 per cent which is markedly above the 3.9 per cent hospital incidence of abnormal presentations. The greatest number of these malpresentations (42 per cent) were encountered in patients with uterus didelphys.

5. *Premature Rupture of the Membranes.*—With irregular uterine contour and the increased incidence of fetal malpresentation, an associated increase of premature rupture of the membranes is to be expected. Forty-four per cent of the pregnancies showed premature rupture of the membranes which is almost double the Sloane Hospital rate of 26.2 per cent, but not nearly as high as the 72.7 per cent reported by Kimura.[9]

6. *Surgical Complications.*—Not infrequently, complications arise during the course of these pregnancies which demand surgical intervention. These are met most commonly in patients with different varieties of duplication of the uterus, notably the bicornate uterus. The nonpregnant horn can swing posteriorly, and besides being a source of serious dystocia, may become twisted and incarcerated[2] and give rise to the characteristic clinical picture of an acute abdominal catastrophe. Of the four patients presenting surgical complications in this study, three belonged to Group 2 (uterus duplex, double cervix) and one to Group 5 (uterus subseptus). Two of the patients in Group 2 had incarceration of the nonpregnant horn, while the third was subjected to a supravaginal hysterectomy for molar degeneration. The patient with the uterus subseptus had a laparotomy for what was thought to be a tubal pregnancy, but proved to be an intrauterine pregnancy in a septate uterus.

7. *Medical Complications.*—There were five patients who presented one of the following medical complications: Rheumatic heart disease, hypertensive cardiovascular disease, pyelitis and thyrotoxicosis.

8. *Plural Pregnancies.*—Two patients, one in Group 2 (uterus duplex, double cervix) and the other in Group 4 (septate uterus) were delivered of one set of twins each, giving an incidence of 1 in 73 pregnancies. In neither of these pregnancies was there any suggestion of superfetation, as has been reported by several authors.[1, 6]

9. *Site of Pregnancy.*—This could be determined correctly in only 13 patients having the duplex or septate type of uterus. In eight patients it was definitely placed on the right, and in five, on the left side. In none of these patients having more than one viable infant was there any evidence

of alternation of the site in successive pregnancies. It is of interest that Smith[15] reports the preponderance of such pregnancies on the right side, although he found alternation of site in consecutive pregnancies.

Complications of Labor

1. *Premature Labor.*—This is said to occur more frequently in patients with congenital uterine anomalies. The predisposing factors are believed to be the same as those already outlined for abortion. In Miller's[10] collected series the incidence was 10.4 per cent. Of the patients with viable pregnancies, 15.2 per cent went into premature labor, which is higher than the Sloane Hospital rate of 6.8 per cent. The incidence of premature labor showed no great variance between the different groups.

2. *Length of Labor and Primary Intrauterine Inertia Intra Partum.*—There were 77 deliveries observed at the Sloane Hospital in pregnancies associated with congenital deformities of the reproductive tract. Of these, 27, or 35 per cent, resulted in cesarean section (Table VI). Precipitate labor was observed in 9.2 per cent, which shows no great variation from the Hospital rate of 6.5 per cent. Uterine inertia (intra partum) was observed in 20.3 per cent, which shows a marked increase over the Hospital rate of 3.2 per cent. This conforms with the findings of other authors.[2, 10] It is likely that the incidence of uterine inertia intra partum in his series would have been even greater were it not for the very high cesarean section rate. Group 3 (uterus duplex) contained the greatest group of cases of uterine inertia intra partum.

TABLE VI. LENGTH OF LABOR IN 77 PREGNANCIES OBSERVED AT SLOANE HOSPITAL

	NO LABOR CESAREAN SECTION	PRECIPITATE LABOR LESS THAN 3 HOURS	NORMAL DURATION OF LABOR	PROLONGED LABOR OVER 30 HOURS. UTERINE INERTIA	CESAREAN SECTION AFTER TRIAL OF LABOR. ADEQUATE PELVIS. UTERINE INERTIA	TOTAL
Group 1	7	2	13	1	0	23
Group 2	0	1	2	0	1	4
Group 3	4	2	8	3	2	19
Group 4	2	0	1	0	0	3
Group 5	0	0	2	0	0	2
Group 6	1	0	5	0	1	7
Group 7	0	0	0	0	0	0
Group 8	1	0	8	2	0	11
Group 9	8	0	0	0	0	8
Total	23	5	39	6	4	77

Cervical dystocia was reported in 2.5 per cent of these deliveries, as compared to the "normal" 0.8 per cent incidence.

It is interesting to record that in a few of these patients the tardy inefficient labor was the first clue in establishing the diagnosis of the abnormality.

3. *Retained Placenta—Uterine Inertia, Third Stage.*—Failure of separation of the placenta has been ascribed to irregularities in the contour of the organ, to its insertion to a septum, and to the faulty contraction of a poorly formed fundus. Retention of the placenta, after delivery of the infant, was encountered in 9 per cent of deliveries and manual removal was required.

4. *Postpartum Hemorrhage.*—Loss of over 500 c.c. of blood after the third stage of labor occurred in only 5.2 per cent of the pregnancies. In none of

them was the hemorrhage severe enough to warrant uterine packing. However, when compared to the Hospital incidence of 0.4 per cent, this indicates the increased tendency for the uteri of these patients to contract inefficiently. Falls[5] found a much higher incidence of blood loss.

5. *Retained Secundines.*—In 12.9 per cent of these pregnancies curettage was done one to three months following delivery for retained secundines. When one compares this figure to the 0.8 per cent which represents the Sloane Hospital incidence of retained secundines, this then becomes still another complication peculiar to these abnormalities. Group 1 (didelphys) and 3 (uterus duplex) showed the greatest incidence of retained placental fragments.

6. *Mechanical Obstructions to Fetal Descent.*—In no case in this series did the nongravid horn obstruct descent of the fetus as has been described by others.[1, 2, 14] However, in 12.9 per cent of the deliveries, the vaginal septum required incision before delivery could be effected. This complication was almost restricted to those cases of septate vagina (Group 8).

No patient in this study suffered rupture of the uterus as described by Hall, due to poorly formed musculature and protracted labors. However, on three occasions, cesarean section was performed for tonic uterine contractions.

Maternal Mortality, Morbidity and Injury

There were no instances of maternal mortality in this series. Falls[4] reports 1.9 per cent maternal mortality and Taylor[17] 1.5 per cent in pregnancies associated with congenital malformation.

Twenty-four per cent of these deliveries resulted in maternal morbidity compared to the Sloane Hospital morbidity rate of 8 per cent. Although this figure closely approximates that of Smith, it is probably related to the high incidence of operative interference.

Cervical or vaginal lacerations occurred in 11.6 per cent of the deliveries. These were mostly vaginal lacerations and usually were associated with breech delivery.

Fetal Mortality

Fetal mortality included stillbirths and deaths in the neonatal period. The gross fetal mortality in pregnancies associated with congenital anomalies of the genital tract was 19.0 per cent (Table VII). When corrections are made, this figure falls to 8.5 per cent, which is still considerably higher than the corrected fetal mortality at the Sloane Hospital (0.9 per cent).

TABLE VII. INFANT MORTALITY

	NO. OF INFANTS	DEATHS	FETAL MORTALITY PER CENT
108 pregnancies Uncorrected total	110	21	19.0
Corrected for 9 infants under 1,500 grams, leaving	101	12	11.8
Corrected for 2 infants with congenital defects incompatible with life, leaving	99	10	10.1
Corrected for 6 cases of premature separation of placenta, leaving	93	8	8.5

Method of Delivery and Presentation Related to Fetal Mortality

Forty-nine and one-half per cent of the pregnancies terminated spontaneously. There were 4 fetal deaths in this group. Two of these infants weighed between 2,000 and 2,500 grams and died in the neonatal period. The remainder were sudden unexplained intrauterine fetal deaths, an occurrence

which has been observed by Falls and ascribed to the poor vascularization of the placenta with resulting fetal anoxia.

When a careful analysis of the entire series is made in regard to the particular method of delivery (Table VIII), it becomes evident that essentially 50 per cent of all deliveries were of the operative type. This is significantly higher than the 20 per cent operative delivery rate in our clinic.

TABLE VIII. METHOD OF DELIVERY RELATED TO TYPE OF ABNORMALITY AND FETAL MORTALITY

METHOD OF DELIVERY	OVER-ALL IN-CIDENCE (PER CENT)	TYPE OF ABNORMALITY—INCIDENCE (PER CENT)									COR-RECTED FETAL MORTAL-ITY PER CENT
		1	2	3	4	5	6	7	8	9	
Normal spontaneous delivery	49.5	27.5	83.3	56.5	71.4	90.0	55.5	0	33.3	0	7.3
Cesarean section	27.2	31.0	8.3	26.0	28.5	0	22.2	0	16.6	100.0	0
Assisted breech	8.1	6.8	8.3	4.3	0	10.0	0	0	33.3	0	14.2
Breech extraction	4.5	17.2	0	0	0	0	0	0	0	0	33.3
Low forceps	6.3	6.8	0	12.9	0	0	11.1	0	8.3	0	0
Midforceps	2.6	10.3	0	0	0	0	0	0	0	0	0
High forceps	0.9	0	0	0	0	0	11.1	0	0	0	100.0
Version and extraction	0.9	0	0	0	0	0	0	0	8.3	0	100.0
Corrected fetal mortality per cent		5.5	7.3	10.0	0	11.1	22.2	0	9.0	0	

Cesarean section was the procedure of choice in the majority of operative deliveries, accounting for a little more than one-fourth (27.2 per cent) of the total number of the cases. Most of the cesarean sections were of the elective type. However, 15 per cent of these patients were allowed a trial of labor before being delivered abdominally. It is interesting to note that the cesarean section rate was approximately eight times as high as our Clinic rate (3.6 per cent).

The number of deliveries terminated by low and midforceps extractions comprised 6.3 and 2.6 per cent of the total, respectively. These figures compare quite favorably with the Clinic incidence of 9.9 and 3.5 per cent. When corrections are made for fetal mortality, this type of operative interference was not associated with any fetal loss.

Breech delivery was associated with a 16.6 per cent fetal mortality which is again a considerably higher figure than our Clinic rate of 4.5 per cent. In uncomplicated breech delivery, however, the fetal loss was 14.2 per cent, but when extraction was employed, as it was in more than one-third of the breech deliveries, the mortality rose to 33.3 per cent.

Version and extraction and high forceps made up almost 2 per cent of the total number of deliveries and were associated with 100 per cent fetal mortality.

It is impossible from our data to relate fetal mortality to pelvic types. Inasmuch as this series extended over a period of 25 years, different classifications were used at periodic intervals.

The fetal mortality relating to the type of presentation is shown in Table IX.

TABLE IX. FETAL MORTALITY RELATED TO PRESENTATION

FETAL MORTALITY	VERTEX PRESENTATION	BREECH PRESENTATION	TRANSVERSE PRESENTATION
Incidence of	82.4%	14.8%	2.7%
Gross fetal mortality per cent	16.4%	37.5%	0%
Corrected fetal mortality per cent	7.4%	16.6%	0%

Fetal Mortality Related to Type of Congenital Anomaly

When the fetal mortality was analyzed as to the type of congenital abnormality, no significant conclusions could be drawn. The mortality appeared to be related more to the presentation and the method of delivery. There was no fetal loss in Group 9 (vaginal stricture) all the patients being delivered by cesarean section. Group 4 (uterus septus) likewise had no fetal deaths. This may be accounted for by the fact that there were no breech deliveries or other operative vaginal deliveries in this group. Group 6 (arcuate uterus) had the highest fetal mortality in our series (22.2 per cent). This was a small group and contained one high forceps and one unexplained sudden intrapartum fetal death.

Fetal Size

Twenty-five per cent of the infants weighed 2,500 grams or less and 59 per cent weighed less than 3,000 grams (Table X). This is related to the high incidence of prematurity in this series. It is impossible from our data to evaluate by the other accepted fetal measurements of prematurity the true number of premature infants in this study. We must conclude that mothers with these congenital abnormalities tend to give birth to smaller infants. Whether this is due to restricted placental growth on a mechanical basis or suggestive of prematurity is a matter of conjecture. The fetal mortality, as one would expect, is higher in the infants below 3,000 grams.

TABLE X. FETAL WEIGHT RELATED TO TYPE OF ABNORMALITY AND FETAL MORTALITY

WEIGHT IN GRAMS	TYPE OF ABNORMALITY									TOTAL NO. OF INFANTS	CORRECTED FETAL MORTALITY PER CENT
	1	2	3	4	5	6	7	8	9		
Less than 1,499	3	1	2	2	1	0	0	0	0	9	0
1,500-1,999	2	0	0	0	0	0	0	0	0	2	0
2,000-2,499	4	1	2	0	0	1	0	2	0	10	20.0
2,500-2,999	12	2	4	2	1	2	0	4	1	28	7.1
3,000-3,499	4	0	8	1	0	0	0	2	5	20	10.0
3,500-3,999	2	0	4	0	0	4	0	2	1	13	7.6
4,000 and over	0	0	0	0	0	1	0	0	0	1	0
Unknown	0	9	4	2	8	1	0	2	1	27	3.7
Total	27	13	24	7	10	9	0	12	8	110	

Fetal Abnormalities

There were two fetal abnormalities in this series, both incompatible with life. One infant was hydrocephalic, another had multiple abnormalities including polydactylism. This high incidence has been reported previously.[3, 12, 15] We encountered no infants with congenital amputations.

Comment

Early diagnosis of congenital uterine and vaginal anomalies is the keystone to careful antenatal supervision and proper management of the preg-

nant patient. The possibility of these malformations must always be borne
in mind, for not infrequently they are overlooked and are discovered only
when subsequent complications arise. There is a definite increase in the
incidence of obstetrical complications in these patients (Table XI). Late
recognition may present an embarrassing situation to even the most skilled
obstetrician.

TABLE XI. PREGNANCY ASSOCIATED WITH GENITAL ABNORMALITIES AND "NORMAL"
PREGNANCY COMPARED

	PREGNANCY ASSOCIATED WITH CONGENITAL ABNORMALITIES OF THE GENITAL TRACT	"NORMAL" INCIDENCE (FROM SLOANE HOSPITAL 1933-1942)
Corrected abortion rate	16.5%	5.6%
Viable birth rate	66.4	93.1
Term birth rate	56.1	85.0
Abruptio placentae	5.5	1.2
Unexplained vaginal bleeding	7.4	1.9
Toxemia	11.1	14.2
Hydramnios	0.8	0.6
Breech and transverse presentations	17.5	3.9
Premature rupture of membranes	44.0	26.2
Premature labor	15.2	6.8
Precipitate labor	9.2	6.5
Intrapartum uterine inertia	20.3	3.2
Cervical dystocia	2.5	0.8
Operative deliveries	50.0	20.0
Uterine inertia, third stage	9.0	1.9
Postpartum hemorrhage	5.2	0.4
Curettage for retained secundines	12.9	0.8
Corrected fetal mortality	8.5	0.9

The management of these patients begins in the early antenatal period.
The increased tendency to abortion calls for unusual conservatism in prophy-
laxis and therapy. Vaginal bleeding should never be interpreted as decidual
shedding from a nonpregnant horn, but must be considered as indicating a
threatened abortion and treated as such. Strict surveillance must be con-
tinued in later pregnancy, for late abortion and premature rupture of the
membranes are not uncommon. One must remember that, owing to improper
or incomplete fusion of the Müllerian ducts, the cervix may be poorly formed,
the uterine musculature may be irregularly disposed and poorly vascularized,
and the stroma may be inadequate.

During labor the patients should be observed very closely because of the
possibilities of a weakened uterine musculature. The problem of uterine
rupture, although a rare occurrence, is to be anticipated. In our series it
was conspicuous by its absence; however, on three occasions tetanic uterine
contractions necessitated cesarean section. Uterine inertia may be anticipated
and, in such cases, delivery can be terminated by cesarean section if other
conservative measures fail. Some authors have expressed great concern about
the condition of the infant in utero during labor,[5] stressing the necessity of
a cesarean section if the fetal heart tones become irregular or continue at a
rapid rate. Before delivery of the infant, postpartum hemorrhage and uterine
atony should be anticipated and precautions taken.

In cases of vertex presentations with an adequate pelvis, delivery may
be allowed to proceed in a normal manner. In our series approximately half
the deliveries were of the normal spontaneous type. There were two un-
explained sudden intrauterine fetal deaths in this group which is in accord
with the findings of other authors; however, this increased fetal mortality

is not of sufficient proportion to warrant a delivery by cesarean section, especially when uncomplicated vaginal delivery is anticipated.

The mortality was quite high when the fetus presented by the breech. In such cases it would seem that cesarean section would be the procedure of choice to increase the fetal salvage. Likewise, transverse presentations would best be treated by abdominal delivery. Here it might be significant to record that although a little more than one-fourth of the deliveries were terminated by cesarean section, there was no fetal loss attributed to this procedure. If one considers these abnormalities as complications of pregnancy and labor per se,[17] cesarean section prerequisites become more lenient, especially if still another complication, though minor, be superimposed.

Operative procedures requiring high and midforceps and version and extraction are to be wholeheartedly deprecated and condemned for they carry a high fetal mortality. Furthermore, since most of these patients tend to deliver premature and smaller infants, any of these previously mentioned procedures would greatly minimize the chances of fetal survival. As stated earlier, cesarean section would be a far better substitute.

In the third stage of labor the placenta may fail to separate, for manual removal was a relatively frequent finding in our series. Likewise, in several instances, postpartum hemorrhage was of sufficient proportion to require transfusion and shock therapy. Besides keeping these two important complications in mind, it must be remembered that occasionally there may be considerable postpartum bleeding from the accessory horn due to the disposal of the heavy decidua, and this occurrence may cause seriouus concern. Curettage for retained secundines was not uncommon in this series.

When these pregnancies and labors were analyzed as to the particular type of abnormality, no definite deductions could be made. The reclassification into small groups detracted from their significance, and the statistics were not consistent enough to indicate a better prognosis for pregnancies associated with a specific type of congenital abnormality.

The maternal salvage in this series does not warrant elective sterilization in these patients as advised by other investigators.

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HODGKIN'S DISEASE IN PREGNANCY WITH A REPORT OF TWELVE CASES*

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HODGKIN'S[1] description in 1832 of the condition which bears his name was not complete. It was more fully described in 1856 by Wilks,[2] who gave it the name by which it is now known. The disease was also called pseudoleukaemia, lymphogranulomatosis, and lymphogranuloma malignum. In 1864 Virchow[3] was successful in distinguishing the disease from leukemia, with which it had been confused. The histological picture was first determined by Sternberg[4] but he obscured the situation by describing it as a form of tuberculosis. It remained for Reed[5] in 1902 and Simmons[6] in 1926 to place the knowledge of the condition on a firmer footing by their accurate and careful studies of the pathological findings in conjunction with the clinical histories. Reed concluded her study by saying: "We believe, then, from the description in the literature and the findings in eight cases examined, that Hodgkin's disease has a peculiar and typical histological picture, consisting of proliferations of the endothelial and reticular cells, formation of lymphoid cells and characteristic giant cells and a gradual increase of connective tissue resulting in fibrosis, and, in most of the specimens, of the presence of great numbers of eosinophiles."

Hodgkin's disease is not a frequent complication of pregnancy according to Palacios Costa, Chavanne, and Zebel Fernandez,[7] who found 5 cases in 30,000 gestations, or an incidence of one in 6,000 pregnancies. Kasdon[8] recently reported 32 cases from the literature including 3 of his own. The purpose of this study is to supplement this number by 20 additional cases found in the literature, and 12 original cases, making a total of 64 cases for this condition through the year 1950.

Case Reports

Twelve cases of Hodgkin's disease complicating pregnancy are herewith described. These are followed by a review of 52 cases from the literature, supplementing the table of 32 published by Kasdon.

CASE 1.—F. P., white, para ii, gravida ii, aged 33 years, was delivered in June, 1943, of premature twins in the twenty-sixth week of pregnancy. Four months later a biopsy of an enlarged node established the diagnosis of Hodgkin's disease. X-ray therapy was instituted. In 1947, in the fourth year of her disease, she again became pregnant and was delivered normally in August of a normal full-term male infant whose subsequent development was normal. The patient remained subjectively well until July, 1948, when she suffered a relapse. Paraplegia developed and she died in December, 1948, five years after the onset of her illness.

CASE 2.—H. C., white, para viii, gravida viii, aged 37 years, had had seven normal pregnancies before Hodgkin's disease developed. The disease became clinically evident and was established by biopsy in June, 1945. She received x-ray treatments promptly with good results. In December, 1946, when lymph node enlargement recurred, nitrogen mustard was given. Three months later she became pregnant and had a normal delivery in October, 1947. The immediate postpartum course was uneventful. Late in 1948 she had a recurrence of Hodgkin's disease and died on Oct. 16, 1948, three years after the onset of the disease.

CASE 3.—V. H., white, para ii, gravida iii, aged 32 years had had two pregnancies which had terminated in full-term normal deliveries. However, in December, 1945, when she was two and one-half months pregnant, she was so ill that she sought medical advice. In February, 1946, she noticed for the first time a swelling in the neck followed shortly by abdominal pain and a spontaneous abortion at approximately four and one-half months. During this time her disease became quite active. A biopsy revealed Hodgkin's disease. She was given roentgen therapy with excellent results. In September, 1946, she complained of anorexia, fever, night sweats, and epigastric distress, which became progressively worse until her admission to St. Vincent's Hospital in February, 1947. Physical examination showed axillary adenopathy, an enlarged liver, and bilateral pleural effusion. She received a course of nitrogen mustard therapy, and several chest taps were performed. She was discharged to the clinic as improved. In May, 1947, she was readmitted suffering from generalized adenopathy, hepatomegaly, and bilateral pleural effusion. She again improved on supportive measures, thoracocentesis, and a course of nitrogen mustard therapy. The last admission was in July, 1947, with recurring complaints of weakness and dyspnea. Generalized adenopathy was again noted. Fluid had accumulated in both pleural spaces, abdomen, and extremities. On the forty-second hospital day she went into coma and died, eighteen months after the clinical onset of her disease.

CASE 4.—R. F., white, para i, gravida i, aged 36 years, had been delivered by cesarean section in October, 1945. The postoperative course was uneventful, and she was discharged on the tenth day. After returning home she noticed a dragging sensation of the right arm which was considered insignificant by her psysician. Two months later, however, she became aware of a swelling of the right supraclavicular region; four months later, in April, 1946, a biopsy revealed Hodgkin's disease. She received intermittent roentgen therapy for fourteen months. In September, 1947, she was admitted to St. Vincent's Hospital, complaining of dyspnea, orthopnea, and general lassitude of three months' duration. Examination showed enlarged cervical glands and right pleural effusion. A course of nitrogen mustard therapy was given and moderate improvement noted. On her second and last admission in October, 1947, she complained of epigastric and left chest pain and severe cough. There was pleural effusion in the right chest, and fluoroscopy revealed an abscess in the right lung and an esophagobronchial fistula. The patient failed rapidly and died Jan. 10, 1948, two years after the onset of the disease. The child is normal and healthy.

CASE 5.—D. T., white, para iii, gravida iii, aged 24 years, had her first child in 1940 and her second in 1942. The onset of Hodgkin's disease was approximately August, 1943. The diagnosis, however, was not established until February, 1945, when a biopsy was done. X-ray therapy was instituted and a satisfactory remission followed. In 1948 she was delivered of a full-term normal baby girl and enjoyed a normal postpartum course. In June, 1949, a node appeared in the left groin.

CASE 6.—M. M., white, para i, gravida i, aged 26 years, gave birth to a normal baby girl in January, 1949. Since the postpartum recovery was slow, a thorough physical examination was made and cervical adenopathy was disclosed. A chest x-ray revealed an enlarged mediastinum. A biopsy established the diagnosis of Hodgkin's disease, and x-ray therapy was administered. All nodes disappeared, and at present the patient is enjoying a satisfactory remission.

CASE 7.—M. R., white, para i, gravida i, aged 18 years, had been perfectly well until December, 1946, when she noticed a swelling in the right side of the neck just above the clavicle. The mass grew slowly. In the second month of pregnancy, June, 1947, she visited a prenatal clinic where a gland was excised and revealed Hodgkin's disease. Subsequently several additional nodes were found in the neck. Her pregnancy, however, was uneventful. After a labor of seven hours she was delivered normally of a living, healthy, normal female infant weighing 6 pounds, 13 ounces. Her postpartum course was uneventful. She has been receiving roentgen therapy with good results. As of September, 1949, she remains well and is desirous of a second baby. The infant, meanwhile, continues healthy and normal.

CASE 8.—E. H., white, para i, gravida i, was 26 years of age. The first evidence of Hodgkin's disease was noted in November, 1947, when a chest film taken because of an upper respiratory infection revealed a mediastinal mass. A biopsy of a supraclavicular gland disclosed Hodgkin's disease. Roentgen therapy was applied to the chest, and the mediastinal mass cleared. In March, 1948, she was admitted to St. Vincent's Hospital because of signs relating to the central nervous system, such as transient periods of unconsciousness and spontaneous twitchings of the extremities. One week prior to admission she had a spontaneous abortion of a 2½ months' fetus. Biopsy of an axillary node confirmed the diagnosis of Hodgkin's disease. In spite of nitrogen mustard therapy, repeated transfusions, and experimental extract therapy, her course was progressively downward; and she died on the forty-fifth hospital day of generalized peritonitis secondary to a ruptured tuboovarian abscess.

CASE 9.—A. M., white, para i, gravida i, aged 33 years, noted the appearance of nodes in the right side of the neck in the second month of pregnancy, August, 1948. Gradually nodes developed in the left side of neck. The only symptom was low back pain. Pregnancy and labor were uneventful. Biopsy revealed Hodgkin's disease. X-ray therapy was instituted in January, 1950. Despite x-ray therapy the general condition of the patient deteriorated. She developed jaundice and persistent high fever in June, 1950. This has persisted on and off to date.

CASE 10.—B. S., white, para i, gravida i, aged 29 years, on Feb. 12, 1950, two weeks following normal pregnancy and labor, noticed swelling of neck. The general swelling subsided spontaneously except for one lump at the base of the neck which persisted and then began to enlarge. A month later she began to tire easily and developed pruritus and sweats. A biopsy revealed Hodgkin's disease. When we saw her in May, 1950, she had many nodules in the neck and enlargement of the mediastinum. She was treated with triethylenemelamine. Nodes have all disappeared and the patient states she feels well.

CASE 11.—M. Mc., white, para i, gravida i, aged 30 years, noted the onset in the fifth month of pregnancy (August, 1949) with sweats and nodes in the left side of the neck. A chest plate revealed an enlarged mediastinum. Biopsy revealed Hodgkin's disease. She was delivered normally of a full-term child Dec. 4, 1949. She received x-ray therapy in January and February. A plate was then made and mediastinum appeared normal. In one month nodes appeared in the right side of neck, concomitantly she developed marked fatigue. Triethylenemelamine was started April 17, 1950. The nodes disappeared and patient regained her usual vitality.

CASE 12.—M. M., white, para i, gravida i, aged 30 years, noted the onset in October, 1949, in the fourth month of her pregnancy, with hemoptysis, fever, cough, and chest pain. She was delivered normally in May, 1950. Biopsy done June, 1950, revealed Hodgkin's disease. A chest plate revealed a widening of the mediastinum. Triethylenemelamine was administered June 17, 1950. By July 12 symptoms had subsided and the mediastinal mass began to shrink.

Discussion

Hodgkin's disease is a comparatively rare complication of pregnancy. Up to the present time the exact nature and causation of Hodgkin's disease remains a matter for conjecture. Very little has been written concerning the management of pregnancy complicated by this condition, and many authors do not mention the complication in their texts. Berkeley and Bonney[39] in 1913 stated that "Hodgkin's disease may first declare itself during pregnancy, or pregnancy supervening upon it, the course of the disease may be much accelerated." They felt that abortion is very common and that the anemia concomitant with the process may lead to retroperitoneal and postpartum hemorrhage. They felt that pregnancy should be terminated.

In a review of the literature and a study of the 52 reported cases of pregnancy complicated by Hodgkin's disease it was found that 22 of the women dated the onset of their disease from some pregnancy. Labor in all cases was normal, no postpartum hemorrhages occurred, and uterine bleeding was practically nil. Exacerbations of varying degrees of severity occurred in 32 cases, 12 during pregnancy and 21 after parturition. There were 18 spontaneous abortions which were not considered related to Hodgkin's disease; there is no evidence that this complication leads to its increased frequency. In 9 cases the pregnancy was interrupted from the twenty-sixth to thirty-fourth week, by hysterotomy and other methods not mentioned. One patient had a medical induction, and one patient was delivered by cesarean section because of massive edema of the vulva.

In the 52 cases reported in the literature the age of 42 parturients could be established. Twenty-eight were in the 18- to 29-year-old group, and 14 in the 30- to 39-year-old group. The youngest patient was 18 years and the oldest was 39 years of age. The oldest parturient in our group was 37 years of age. Herz[15] believes that the disease is most frequent between the ages of 30 and 50, and Epstein[40] states that 92 per cent of the women with Hodgkin's disease between the ages of 30 and 50 years survive three or more years.

The incidence of pregnancy seems to be greatest between 20 and 30 years of age, and this fact accounts for the 28 cases reported in this group out of a total of 42 cases in which the age was stated. An analysis of the number of pregnancies in the reported patients reveals that 16 were primigravidas, 14 were gravida ii, 4 were gravida iii, 3 were gravida iv, and 3 were gravida v. In our series we had one case of gravida viii. There is apparently no significance in the relation between Hodgkin's disease and the number of pregnancies.

We find that 27 cases were diagnosed as Hodgkin's disease before gestation, 21 during gestation, and 3 following gestation. In one case the time of onset was not known, whereas 40 per cent of the total number dated the onset as occurring during gestation. Six of the women had 2 pregnancies, 5 had 3 pregnancies, and one had 4 after the diagnosis of Hodgkin's disease had been made. Fertility apparently is not affected by the disease, and there appears to be no interference with ovulation. The patients did not seem to be adversely affected by their pregnancies and nearly all of them were permitted to continue.

Hodgkin's disease may or may not be transmitted to the offspring of mothers having the disease during the course of pregnancy. However, manifestation of the disease in the infants is most unusual, the great majority having been unaffected. dePalo[27] mentioned a case in which the offspring showed signs of the disease at 2 months and died at 4 months of age. Priesel and Winkelbauer[11] described an autopsy on a 4½-month-old child which disclosed involvement of all organs. Von Braitenberg[20] reported a case in which signs of Hodgkin's disease first appeared at 1 month of age. He suggested the possibility of transmission of the disease from mother to child across the placenta.

Although this would seem a plausible explanation, it was not substantiated, since there was no evidence that the mother had Hodgkin's disease, and no pathologic changes were found in the placenta. Leutkens[14] reported a case of Hodgkin's disease in a child 33 months old, whose mother died of this condition at 2 months postpartum. Gilbert[41] described a normal living child of 12 years born of a mother with Hodgkin's disease, the oldest child reported in the literature. In a series of 125 patients followed in the Hodgkin's disease clinic at St. Vincent's Hospital there was one patient aged 16 whose mother had died of Hodgkin's disease 2 years before.

TABLE I. DURATION OF LIFE POST PARTUM IN FATAL CASES OF HODGKIN'S DISEASE REPORTED
IN THE LITERATURE

AUTHOR	YEAR	WEEKS POST PARTUM
1. Davis[9]	1911	17
2. Priesel and Winkelbauer[11]	1926	Shortly after delivery
3. Luetkens[14]	1934	12
4. von Braitenberg[20]	1938	Shortly after delivery
5. Parade[28]	1940	16
6. Ritvo[31]	1940	17 *years* after delivery
7. Parade[28]	1940	1
8. Palacos Costa, Chavanne, and Zebel Fernandez[7]	1945	2
9. Perrier[35]	1945	156
10. Perrier[35]	1945	12
11. Perrier[35]	1945	260
12. Kasdon[8]	1948	1
13. Harris, W. H., Jr.[42]	1948	5
14. Hennessy and Rottino	1947	260
15. Hennessy and Rottino	1947	78
16. Hennessy and Rottino	1948	72
17. Hennessy and Rottino	1948	88
18. Hennessy and Rottino	1949	6

Table I shows how long after delivery death occurred in the 18 cases reported. The longest period of survival is seventeen years; one patient lived five years, one for three years, three for one year. The shortest period was seven days. A noticeable fact is that there were no deaths before evacuation of the uterus. From Table I it cannot be stated that pregnancy prolongs the life of the patient with Hodgkin's disease. The longer life may be explained by her better physical condition which in the first instance made pregnancy possible. Moreover, the course of the disease in those patients in whom pregnancy was artificially terminated did not differ from its course in those in whom pregnancy went to term. The case reports of Davis, Kushner,[33] von Braitenberg, and Parade present postmortem examinations. In none of the patients were the ovaries or uterus involved by Hodgkin's disease. Our study of the autopsy specimens in two cases supports these findings.

In the management of pregnancy during Hodgkin's disease the question of interruption of the pregnancy has, for years, been in the forefront. Adair[29] felt that the prognosis was unfavorable. Of the thirty-two authors who have presented cases seven recommended interruption and five advised against it. Dyes[25] felt that the response to x-ray therapy should determine the indication for interruption and that conservation of the fetus is advisable whenever possible. Parade[28] believed that although the process may be aggravated by pregnancy nevertheless routine interruption should not be advised. Perrier[35] stated that "there do not exist, in general, medical indications to interrupt a pregnancy in the course of lymphogranulomatosis." As we see it, Hodgkin's disease is rarely, if ever, aggravated by pregnancy; hence interruption of the preg-

nancy is rarely indicated. McGrath[13] of Dublin reported a case occurring in 1930; as part of the treatment, which included roentgen therapy, the patient was given a serum from chickens infected with lymphogranulomatous material from other patients. She had no reaction to the injections. The serum treatment in this case, as far as can be ascertained, was entirely devoid of results. Surgical removal of the glands must necessarily be incomplete; in fact, it is very ineffective, and (except for diagnostic purposes) worse than useless.

In some cases roentgen therapy with adequate shielding is apparently an effective method of treating Hodgkin's disease associated with pregnancy. It produces a dimunition in the size of the glands, and in some cases their complete disappearance. Adequate shielding prevents radiation injury to the fetus. All of the cases, except three, in our series received nitrogen mustard. We found that about 70 per cent of the patients showed objective improvement and about 90 per cent subjective response. Remissions last for only a few weeks and in some instances as long as two years, the average being four to six months.

Summary and Conclusions

1. Hodgkin's disease has been known for over a hundred years, but its management in pregnancy includes only fifty-two cases, reported by various obstetricians scattered throughout the world. In each case diagnosis was confirmed by histologic study, although in some cases it may be made clinically, with comparative ease. The only positive diagnosis is based on the histologic study of an excised gland, preferably from the cervical or axillary region. Our study of twelve cases is herewith presented.

2. Symptoms may exist for years; one patient had symptoms for seventeen years. The cardinal symptom in the typical case is the painless enlargement of the cervical lymph nodes. However, the primary swelling may be elsewhere, and the cervical glands may never be affected.

3. Interruption of pregnancy complicated by Hodgkin's disease is not indicated, as borne out by a study of our own cases and by a careful review of the literature.

4. Hodgkin's disease complicating pregnancy does not apparently affect ovulation, fertility, incidence of abortion, antepartum or postpartum hemorrhage.

5. Pregnancy has no apparent effect on the over-all incidence of exacerbations compared with pregnancy in a group of patients not suffering with Hodgkin's disease.

6. Except for three reported cases of Hodgkin's disease in young infants, all other viable children born of mothers with Hodgkin's disease have been found to be free of the disease.

7. Roentgen therapy and other forms of therapy used in the treatment of Hodgkin's disease exert no untoward effect on pregnancy or the fetus.

8. All received nitrogen mustard therapy except three who were treated with triethylenemelamine.

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Discussion

DR. ANTONIO ROTTINO (By invitation).—At St. Vincent's hospital we have been interested in this disease for the past seven years and during that period have studied and followed approximately 200 cases. The 12 cases which Dr. Hennessy reports were collected from this series.

In analyzing our data we noted that there were three behavior patterns.

The first is typical of the patient whose first indication of trouble is enlarged lymph nodes. When biopsy confirms the suspicion of Hodgkin's disease treatment will induce a remission lasting from six months to a year. Relapse occurs, treatment is again given and again a remission takes place, but this time it will be of shorter duration than the first remission. From this point on remissions are increasingly short and relapses correspondingly more frequent, until death occurs. Persons with this behavior pattern will usually live for one to five years, during which time pregnancy and normal delivery of an apparently normal child may take place. In such cases the pregnancy does not affect the course of the disease process for either better or worse.

There are a few cases in the second group which, when properly treated, have lengthy remissions; medical history records some as long as 35 years. We have several patients

who became pregnant early in the course of the disease and who, to date, after a span of two or three years, have had no relapse. Such persons have the disease in a mild form and pregnancy has no more effect upon it than does any other routine indisposition.

Finally, we find, in the third group, patients who suffer a rapid progression of symptoms after onset of the disease, and death usually occurs within six months. In these instances a diagnosis of "acute Hodgkin's" is usually made, but careful culling of the clinical histories shows that for a long period of time there had been obscure symptoms of conditions difficult to diagnose and often dismissed as "grippe." Sometimes these patients had suffered from unexplained backaches, others recall small swellings in the neck which had disappeared spontaneously without any particular attention having been paid to them. Thus, there has been a period of unknown duration, but quite often protracted, during which symptoms have been minor in nature, before the final and true picture emerges. We have not as yet had a pregnant patient with this type of the disease, but I feel reasonably sure there are such. Probably all patients who are stricken down "suddenly" with Hodgkin's disease during or soon after pregnancy have actually harbored this undiagnosed form for many years.

The wherefore of these variations in the course followed by Hodgkin's disease is not at present known, but most probably the degree of virulence of the causative agent and the immunological response of the individual patient involved have something to do with the matter. We have noted during the course of our rather extensive studies of the pathological changes in Hodgkin's disease tissue a progression of changes which to some extent are correlative with the changes in clinical status of patients.

The earliest histological picture is characterized by diffuse hyperplasia of lymphocytes and the presence of reticulum cells with prominent nucleoli. In my opinion this reticulum cell is pathognomonic of Hodgkin's disease, while the abnormal number of lymphocytes is indicative of stimulated operation of the defensive mechanism.

As the disease progresses the following things happen: the lymphocytes gradually disappear and the reticulum cells increase in number and become quite bizarre in form. The Sternberg-Reed cell is an example of the latter phenomenon.

As the disease becomes more advanced the lymphocytes disappear almost completely, the reticulum cells diminish in number, and the node becomes replaced by fibrous tissue.

The patient's response to treatment parallels these progressive changes. Those who respond best to treatment do so when the lymph node is characterized by lymphoid hyperplasia; the patients who respond least are those in whom the node has become fibrous or in whom a Hodgkin's sarcoma has intervened. To repeat, when the lymph node reaches the stage of either fibrosis or malignancy, then the patient's response to therapy is poor.

We did not have an opportunity to treat any of the pregnancy cases with nitrogen mustard until very recently. One patient was referred to us in her third month, with massive Hodgkin's disease of the neck and of the mediastinum. She received x-ray therapy, after which the mediastinal nodes disappeared to a considerable extent. The lymph nodes in the neck grew larger, however, so we gave her triethylenemelamine, which is a compound having an effect similar to nitrogen mustard and which can be given by mouth. Two such courses during her pregnancy had no effect on the pregnancy. She carried well, the lymph nodes in the neck subsided considerably, and in due course she delivered normally. The child is now about 4 months old and is well. Since then we have given the patient triethylenemelamine again with some measure of success.

DR. A. A. GEMMELL (Liverpool, England, by invitation).—My patient, seen about 1925, bears out many of the features which Dr. Hennessy has mentioned. In this patient, a young multigravida, who had had three previous deliveries, the disease was discovered and proved by section during a time when she was not pregnant but was having irregular and infrequent menses. It was treated in those days simply by x-rays, and the glands decreased in size and her general condition improved. She became pregnant and the glands quite quickly appeared to enlarge again. It may have been that she was in one

of these remission phases or advancing phases that have been described. Anyhow, the obstetrician who was looking after her at the time considered that the disease was aggravated by the pregnancy and that pregnancy was terminated. The glands again diminished and she was comparatively well for some time. She had had three sons, and was most anxious to have a daughter and against the advice of her obstetrician she became pregnant again. Again the glands enlarged and because of her great anxiety that this might be a daughter the pregnancy was not on this occasion interfered with. She went to term, was delivered normally of a daughter, and that young lady is now about 26 years old and perfectly healthy. The point that I tried to make, when I looked up the literature at that time, was that Hodgkin's disease is relatively much less common in the female than it is in the male. It appears to originate most commonly in the female during a period when the estrogenic hormone is in decline, namely, in a period of amenorrhea or during pregnancy, and the suggestion occurred to me that if such patients in addition to their ordinary therapy were given estrogens that might help. You will appreciate that this was at a time when endocrine studies were in their infancy and it was impossible to make any detailed study on her estrogenic output. However, acting upon my young enthusiasm, the obstetrician of that day did give her such estrogens as were available and we were all very pleased with the fact that she did survive for six years from the time when the Hodgkin's disease was first diagnosed.

DR. JOHN J. MADDEN.—Reviewing the records at the Brooklyn Hospital covering a period of 15 years, during which time we had about 25,000 deliveries, we found just one patient in whom Hodgkin's disease and pregnancy coexisted. During that time the hospital as a whole had discharged 71 patients with Hodgkin's disease.

Briefly, I would like to give the obstetrical history of this one patient. She married in 1936. She was aged 24. In 1937, one year later, she delivered a normal full-term infant; two years later, in 1938, she had an early spontaneous abortion. This was all before the diagnosis of Hodgkin's disease was made. In 1941 she first noticed nodules in the neck. One of these was removed at that time and the diagnosis was made of Hodgkin's disease. X-ray therapy was started and in December she reported she had missed two periods and examination showed she was about eight weeks pregnant at that time. Consultation was then held and it was decided that this pregnancy should be interrupted, which was done, and she continued her x-ray therapy all through 1942, with rest periods, and did very well. In fact, she did very well up until 1947 and then again reported she had missed two periods and was pregnant again. At that time the x-rays of the chest were negative and no signs of any disease were apparent. She was allowed to go through this pregnancy and had a perfectly normal, easy labor. She was all right for another two years when she complained of dragging and a heavy feeling in the upper left quadrant. At that time the spleen was found to be enlarged and to relieve the symptoms of which she complained the spleen was removed. The spleen weighed 650 grams, at least three times normal size, and was infiltrated with Hodgkin's disease. Following that she made a good recovery, and this year, 1951, which is ten years following the first diagnosis, she is still alive and well and at the last examination she had a few inguinal nodes, which were treated with x-ray therapy and subsequently regressed. She had x-ray therapy for the mediastinal and supraclavicular nodes. She had 4,200 units to the neck and 3,500 units to the chest.

THE PELVIC OUTLET

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IN THE management of the pregnant woman meticulous clinical pelvimetry, especially of the pelvic outlet, is markedly neglected. Therefore, a woman may suffer many hours of exhausting labor before a diagnosis of pelvic contraction is made and intervention adopted. In routine pelvimetry, even by x-ray, measurements pertaining to the pelvic inlet are stressed and little attention is given to the pelvic outlet which is more frequently abnormal, is more accessible and offers the only part of the birth canal from which a general idea of the pelvic architecture may be derived clinically. Stander[1] has said that outlet contraction "probably represents the most common type of abnormality encountered in the American woman" and "more or less serious contraction of the outlet frequently occurs in pelves which appear to be perfectly normal as far as the usual pelvic measurements are concerned." Jellinghaus,[2] in urging pelvimetry of the outlet, stated, "It is so easy and requires no fuss or pain to the patient. Even if a man were too lazy to measure the posterior sagittal he could benefit a lot by just measuring the transverse." With the enthusiasm developed for x-ray pelvimetry the importance of the clinical measurements and palpation of the contours of the pelvis with particular reference to the outlet is being rapidly submerged. In many cases the attending obstetrician is too greatly influenced by the report of the radiologist and fails to give sufficient weight to his own clinical appraisal of the parturient; hence this plea to study more assiduously the pelvis and fetus by clinical methods, correlating these data with x-ray studies when the latter are indicated.

The birth canal has three planes, the inlet, the midpelvic, and the outlet planes, with the midpelvic plane dividing the canal into 2 compartments, the inlet and the outlet. We are concerned in this treatise with the outlet compartment bounded anteriorly by the lower border of the symphysis pubis and the inferior rami of the pubes forming the subpubic arch. Laterally are the levator ani muscles with the ischial spines and the sacrosciatic ligaments in the upper plane and the tuberosities of the ischium and the sacrotuberous ligaments in the lower plane. Posteriorly there are the sacrum, coccyx, and the sacrococcygeal junction.

In estimating the descent of the fetal head during labor it is best to use the station of the biparietal diameter in relation to the birth canal because it is the fetal skull diameter used in determining disproportion, is least affected by molding, and also because the position of the vertex may be so confusing through molding, caput formation, and degree of flexion of the head. When the biparietal is in the inlet compartment, that is, on the level of or just below the

plane of the inlet, it is "engaged and high." When it has reached or is just below the midpelvic plane between the ischial spines it is "mid." When it is traversing the outlet compartment below the plane of the midpelvis, it is "low." Cephalopelvic disproportion at the pelvic inlet is a relatively simple matter and may be determined somewhat mathematically by x-ray pelvimetry but better still by an intelligent test of labor. However, once the head has entered the pelvis and assumes its journey through the outlet compartment many complicating factors must be considered. First, the progressive narrowing which may take place in this area. Then the important aberrations from the normal in the contours of the birth canal caused by angulation of the forepelvis or flattening of the posterior pelvis which may interfere with internal rotation of the head especially in the posterior and transverse occipital positions. Here, too, the forces of labor, the strength of the uterine contractions and abdominal muscles assume a more significant role along with the resistance of the soft tissues, especially the levator ani muscles with their pubococcygeal sling. There are no rules for a test of labor in the outlet compartment and one usually feels committed to delivery from below once the head has become engaged, the inlet being considered erroneously so important. The risk to the fetus may increase with descent of the head into the midpelvis and outlet with consequent death of the fetus by improper handling if difficulties are not properly anticipated. Adequate capacity for the reception of the fetal head presenting a globular surface with a diameter of 9.5 cm. is the ideal situation but frequently lacking. Fortunately, however, molding and asynclitism may diminish the presenting surface of the head sufficiently to allow delivery by proper management through a considerably narrowed outlet.

Methods of Clinical Pelvimetry

Measurements are taken and palpation of the pelvis is done at the first visit and repeated with the exception of the vaginal examination two weeks before term. The usual technique is employed for measuring the inlet including the intercristal, the interspinous, intertrochanteric, external conjugate, and when feasible the diagonal conjugate diameters. These latter measurements are important only in a broad sense and allow one to divide the pelves into "large," "medium," and "small." They in no way help in determining accurately the size or architecture of the pelvic inlet. The outlet segment is measured by one of the ingenious pelvimeters designed by DeLee, Williams, Thoms, or Pieri.

Pubotuberous Diameter.—This was originated by Schuman[3] and is measured from the mid-point of the medial aspect of the ischial tuberosities perpendicularly upward to the upper surface of the superior ramus of the pubis, usually about where the pubic tubercle is situated. One cm. is subtracted to allow for the soft tissues. The diameter is usually 11 cm. and gives the length of the forepelvis. It provides a criterion for detecting the funnel pelvis, any pelvis longer than 11 cm. suggesting the funnel type. The latter exerts its effect particularly in the outlet segment and if accompanied by narrow interpubic and intertuberous diameters may cause delay in the descent of the head and possibly arrest in rotation with consequent persistent posterior position or deep transverse arrest. The funnel type is seen frequently in the high assimilation pelvis, and in the anthropoid and dystrophia-dystocia types of individual.

Interpubic Diameter.—This is the width of the subpubic arch and is measured between the inferior rami of the pubis at a point 2 cm., or a thumb-breadth, below the inferior border of the symphysis. One-half cm. is added to allow for the soft tissue thickness.[4] This diameter is usually 6 cm. and permits reception of the fetal occiput, which averages 6 cm., when the fetal head impinges under the arch in the mechanism of birth by extension of the head. Actually measuring the arch is much superior to classifying it as "large," "medium," or "small," or computing its angle in degrees. Narrowing here also indicates angulation of the forepart of the midpelvis and outlet compartment with possible delay in rotation. Also, it may force the occiput to seek a lower plane on the arch for impingement with consequent added strain on the perineum. On the other hand, a wide arch may compensate for a narrow posterior midpelvis.

Intertuberous Diameter.—The plane measured between the mid-point of the medial border of the tuberosities of the ischium with 1 cm. added for soft tissue thickness is the intertuberous diameter. This must be at least 9.5 cm. for reception of the biparietal diameter of the fetal head at the time of delivery. A smaller diameter forces the head toward the anus with danger of a third degree laceration of the perineum. With a narrow intertuberous diameter if forceps are used traction must be exerted well downward to bring the biparietal diameter below the intertuberous to find room in the soft tissues for its reception.
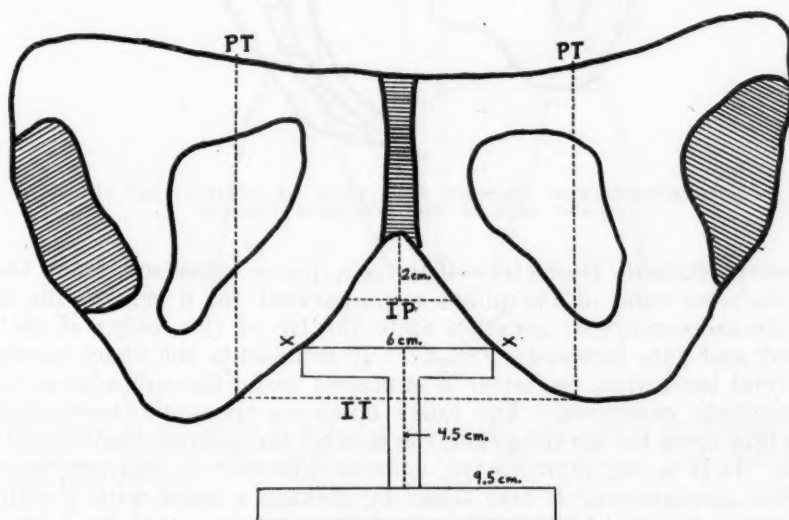

Fig. 1.—Important anterior diameters of midpelvis and outlet and pattern used to locate position of head during extension in narrow outlet.

A simple method of determining the capacity of the subpubic arch for reception of the head is to make a pattern out of cardboard duplicating the size of the fetal head as illustrated in Fig. 1. The pattern consists of an upper horizontal bar measuring 6 cm. and representing the occipital diameter; a lower horizontal bar measuring 9.5 cm. and representing the biparietal diameter; a vertical bar measuring 4.5 cm. from the upper surface of the lower bar to the upper surface of the upper bar and representing the distance from the occipital to the biparietal diameter. Application of such a pattern to the pelvis offered for consideration will tell where the head will have to lie to find room for extension.

Posterior Sagittal Diameter.—This is measured from the middle of the intertuberous diameter to the sacrococcygeal junction. If one uses the special

pelvimeter of Pieri or Thoms, a point posterior to the junction is used and 2 cm. must be subtracted to compensate for the thickness of the bone and soft tissues. Measuring on the index finger with its tip against the sacrococcygeal junction through the rectum is a very satisfactory method.[5] The posterior sagittal diameter is important only if the intertuberous diameter is below 9.5 cm., whereupon it compensates for the narrow transverse diameter when the head is born by extension. The sum of the intertuberous and the posterior sagittal must equal 15.5 cm. or dystocia may exist. If the intertuberous diameter is adequate to receive the biparietal of the fetal head, measurement of the posterior sagittal is really not necessary.
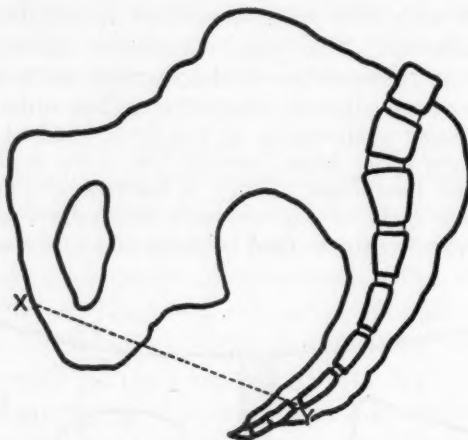

Fig. 2.—XY = pubosacrococcygeal diameter, from point where upper bar of pattern fits into subpubic arch to sacrococcygeal junction.

Pubosacrococcygeal Diameter.—This is a plane measured from the point where the inferior rami of the pubes are separated for 6 cm., to the anterior aspect of the sacrococcygeal junction or to the tip of the coccyx if the coccyx is ankylosed and juts forward (Fig. 2). It represents the space occupied by the flexed fetal head when the latter is impinged under the subpubic arch and is about to undergo extension. The lower down on the arch the occiput must descend to find room for its reception, the shorter the pubosacrococcygeal diameter may be. If it is less than 9.5 cm. definite difficulty in delivery may be expected. This measurement is best taken by making a mark with a skin pencil on each inferior ramus of the pubis where they are separated by 6 cm. Then inserting the index finger into the rectum with its tip touching the sacrococcygeal junction or the tip of the coccyx if the latter is ankylosed, a mark is made on the finger where it reaches the 6 cm. plane between the pubic rami. The desired measurement is then taken directly from the finger. This latter may be facilitated by marking off in centimeters the index finger of the rectal glove used in the measuring process.

Posterior Transverse of the Inlet.—This measurement is taken with the patient lying on her side and is between the most medial aspect of the dimples overlying the posterior superior iliac spines.[6] It is usually 1 cm. less than the intertuberous. If it is below 8.5 cm. one must look for narrowing of the transverse diameter of the pelvic inlet or more likely narrowing of the distance between the spines of the ischium with consequent interference with rotation of the head.

Palpation of the Sacrum and Coccyx.—This is also done with the patient lying on her side. The breadth and projection of the sacrum are noted and

the position, mobility, and length of the coccyx. It is ascertained whether or not a sacrococcygeal platform exists. A narrow sacrum suggests a transverse narrowing of the lower midpelvis. The forward projecting sacrum encroaches on the anteroposterior diameter of the lower part of the outlet segment and may interfere with rotation or with birth of the head by extension. The ankylosed coccyx at right angles to the sacrum constitutes a shelf to impede progress of the head as it approaches the plane of the outlet.

Vaginal Examination.—This completes the clinical appraisal of the birth canal and helps considerably to complement the pelvimetry.

* First, palpation of the symphysis and architecture of the subpubic arch is done to confirm the impression derived from measurement of the interpubic diameter. The narrow symphysis and acute arch support the finding of a narrow interpubic diameter.
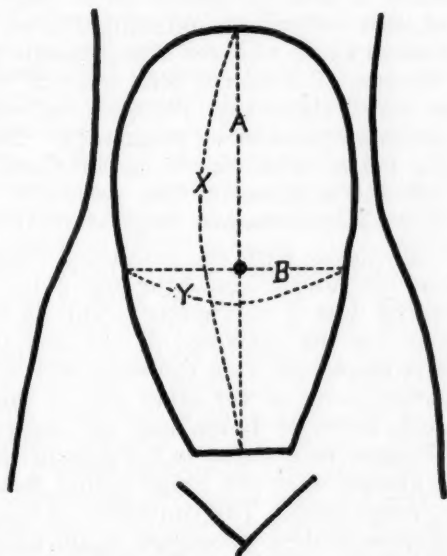

Fig. 3.—Diameters measured to estimate size of pregnant uterus. *A* = vertical length from upper border of symphysis to top of fundus taken with caliper pelvimeter. *B* = transverse diameter level with umbilicus taken with caliper pelvimeter. *X* = vertical length taken with tape measure over convexity of uterus. *Y* = transverse diameter taken with tape measure over convexity of uterus.

The levator ani sling, especially the lowermost sphincterlike pubococcygeus component, is felt and recorded as to thickness, pattern, and elasticity. Firm inelastic levators may offer considerable resistance to the head. A narrow outlet diminishes the hiatus between the pubococcygeal muscles delaying progress of the head and in forceps deliveries necessitating considerable traction unless the pelvic floor is ironed out manually or a liberal episiotomy is done.

The vaginal surface of the sacrum and coccyx is palpated and an appraisal is made of the contour and the projection of the sacrum and its encroachment on the anteroposterior diameter of the outlet. The length and mobility of the coccyx are determined.

The spines of the ischium are carefully felt on either side of the posterior wall of the vagina. If they are unduly prominent and pointed one may suspect narrowing of the transverse diameter of the midpelvis. If they are less than 2 fingerbreadths from the lateral wall of the sacrum there may be narrowing

of the posterior sagittal diameter of the midpelvis. Both of these latter abnormalities would lead to interference with rotation. With the index finger on a spine and the thumb on the curving ramus of the pubis at the same level one may get a good estimate of the anterior sagittal diameter of the midpelvis or the capacity of the forepelvis.[7] Moloy and Steer[7] claim that the interspinous diameter, the subpubic arch, and the posterior sagittal diameter of the midpelvis give more reliable information regarding midpelvic and outlet capacity than the conventional intertuberous and posterior sagittal diameters of the outlet. The intertuberous and the posterior sagittal diameters of the outlet are always greater than the corresponding diameters of the midpelvis.

Estimation of Fetal Size in Utero.—Clinical measurement of the size of the fetus in utero although inexact may be of considerable help in a broad sense especially if supplemented by x-rays interpreted by a skilful radiologist. If the head is unengaged, the occipitofrontal diameter which in 65 to 70 per cent of cases lies transversely above the pelvic brim may be measured directly through the abdominal wall with the usual caliper type of pelvimeter. If this diameter is under the usual 11 or 11.5 cm. the prematurity of the fetus may be judged by applying the law of uniform fetal growth ratios as established by Scammon and Calkins[8] which states that the occipitofrontal diameter will grow 1.2 cm. per month in the last trimester of pregnancy. Estimation of conformity of the fetal head to the pelvic inlet may be ascertained by using Kerr's technique by which the left index finger in the patient's rectum determines the descent of the head effected by pressure from above the symphysis.

Measurements of the uterus with the contained fetus are of distinct value (Fig. 3). The height of the fundus above the mid-point of the upper border of the symphysis is measured with a pelvimeter. This is usually 27 to 28 cm. at term, allowing of course for the thickness of the soft tissues. The horizontal diameter of the uterus is measured from the most lateral point of the uterus on one side to a corresponding point on the other side at the level of the umbilicus. This measurement at term averages 15 cm. and will compensate for any shortening in the longitudinal measurement due to the axis of the fetus lying obliquely in the uterus. If it is greater than the longitudinal measurement it suggests a possible transverse lie of the fetus. The convexity of the uterus along its longitudinal and horizontal axes is then measured, again allowing for the thickness of the soft tissues, with a tape measure. These latter measurements will cause recognition of any forward projection of the uterus which might not be obvious by the straight longitudinal and horizontal measurements. The sum of all 4 measurements ranges from 95 to 105 at full term with the fetus weighing from 5½ to 8 pounds. If the sum is less than 95 the chances are great that the fetus is premature. If the sum is greater than 105 one must consider multiple pregnancy, large baby, hydramnios, or a high unengaged head.

Indications for X-ray Pelvimetry.—X-ray pelvimetry is of invaluable aid to supplement but never supplant clinical measurements. It is particularly indicated in primiparas with floating heads at term; all elderly primiparas; multiparas with a history of previous difficult deliveries; primiparas with breech presentations; and patients with narrow outlets to determine the capacity of the posterior midpelvis which may be quite difficult to ascertain clinically.

Management

Careful attention to the details of clinical pelvimetry and palpation aided when necessary by x-rays will greatly reduce the hazards to the mother and fetus of pelvic delivery. Disproportion cannot be reduced to a mathematical formula. Every case should be given a test of labor. The duration of the

test is determined by progress as influenced by the character, frequency, and rhythmicity of the pains and the condition of the mother and fetus. It is to be remembered that good contractions with normal rhythmicity and pattern, along with molding and asynclitism of the fetal head can effect delivery through the natural channels in many cases where delivery from below was considered very doubtful. Continuous progress in dilatation of the cervix and descent of the head without undue delay in the sequential order of the mechanism of labor warrants conservatism and watchful waiting.

Once the head has traversed the inlet the probability of cesarean section is markedly decreased. However, in cases where there is a combination of a narrow inlet and midpelvis and there has been difficulty in engagement of the head then cesarean section must be seriously considered. When the head has reached the midpelvis the accoucheur is generally committed to delivery from below and knowledge of the midpelvis and outlet is of paramount importance. It is at midpelvis that the head begins its descent through the outlet compartment and simultaneously undergoes internal rotation along with more marked anterior flexion combined with lateral flexion forward producing posterior asynclitism. Narrowing of the subpubic arch anteriorly and/or the interspinous or posterior sagittal diameters of the midpelvis posteriorly may interfere with this flexion and rotation and thus cause dystocia, with mid transverse arrest or persistent posterior position. Anterior positions rarely offer any difficulty. In transverse and posterior positions the decision must be made whether the forces of labor are adequate to effect rotation and delivery or whether intervention will be necessary. If after 20 strong contractions at full dilatation of the cervix a head has not rotated the chances are it will have to be rotated manually or by forceps and too much delay may be disastrous. At full dilatation of the cervix the pubouterine and uterosacral ligaments are stretched out markedly in fan-shaped fashion. Therefore, the longer the second stage the more these ligaments are weakened with consequent danger of cystocele and prolapse. This applies particularly to the elderly primipara. Also at full dilatation the fetus is in greater danger of asphyxiation because of the retraction of the uterus with consequent increased force of contractions together with shrinking of the placental site. However, in the latter instance, it is poor policy to use forceps hurriedly in cases of fetal distress. It is better to try to slow up labor and give the mother oxygen until the fetus has sufficient oxygen to carry on. It is to be emphasized that rotation with forceps should not be attempted at the level of arrest but the head should be pushed to a higher position or, maintaining the original position, traction exerted downward until sufficient room for rotation anteriorly has been reached. Attempts at too early and vigorous rotation may result in lateral sulcus tears from prominent ischial spines, separation of the symphysis, stillbirth, a shocked infant, or serious injury to the maternal soft parts.

Delivery of the head by extension must be accomplished by first drawing the head well down on the arch where the occiput has ample room for impingement as determined by prenatal examination. This may necessitate a wide mediolateral episiotomy to prevent tearing into the sphincter and rectum. Extension must never be attempted until the occiput is projecting well forward under the arch. The coccyx may be displaced posteriorly in the process of delivery with consequent tightening of the pubococcygeus muscle drawing the bundles close to the midline, thereby predisposing to tearing. Pressure upward on the arch may force the anterior part of the pubococcygeus apart with the result that the urethrovaginal bundle of the levators is stretched or lacerated. Intermittent traction simulating nature's timing is, of course, essential. Instrumental intervention before full dilatation invites disaster.

Material and Results

The measurements of 1,000 routine private cases were reviewed to obtain the incidence of narrowing of the outlet compartment and the results are shown in Table I.

TABLE I.   CAPACITY OF OUTLET COMPARTMENT IN 1,000 CASES

Normal	66%
Narrow forepelvis only	19%
Narrow posterior pelvis only	6%
Narrow both fore and posterior pelvis (funnel type)	9%

The narrow forepelvis is considerably more common than the narrow posterior pelvis with ample capacity anteriorly compensating for narrowness posteriorly in a large percentage of cases. The pure funnel type with narrowness in both the fore and posterior pelvis occurred in 9 per cent of the cases. The type of delivery of 250 cases with a normal pelvic outlet segment (Table II) was compared with that of 250 cases with a narrow outlet segment (Table III). Only those patients were included who had been delivered vaginally of full-term babies weighing 6 pounds or more, presenting by the occiput, and uncomplicated except by abnormalities of the outlet compartment.

TABLE II.   DELIVERY IN 250 CASES WITH NORMAL OUTLETS

	PRIMIPARAS (152 CASES)	MULTIPARAS (98 CASES)
Normal	11 cases	16 cases
Low forceps	138 cases	82 cases
Midforceps	3 cases	0 case
For mid transverse arrest	2 cases	0 case
For persistent posterior	1 case	0 case

TABLE III.   DELIVERY IN 250 CASES WITH NARROW OUTLETS

	PRIMIPARAS (133 CASES)				MULTIPARAS (117 CASES)			
	NARROW ANT. PELVIS ONLY	POST. PELVIS ONLY NARROW	NARROW BOTH ANT. AND POST.	TOTAL	NARROW ANT. PELVIS ONLY	NARROW POST. PELVIS ONLY	NARROW BOTH ANT. AND POST.	TOTAL
Normal	0	0	0	0	20	5	5	30
Low forceps	73	17	23	113	45	16	21	82
Midforceps	2	6	12	20	0	0	5	5
For mid transverse arrest	1	4	8	13	0	0	3	3
For persistent posterior	1	2	4	7	0	0	2	2
	75	23	35	133	65	21	31	117

There were no cesarean sections done for narrowness of the outlet compartment alone. "Low forceps" in these statistics means the head is causing bulging of the pelvic floor with the vertex showing at least 2 cm. at the introitus. "Midforceps" means there is no buldging of the pelvic boor but the biparietal diameter is level with or below the spines of the ischium. "Low forceps" does not imply pelvic abnormality but is done in many cases particularly in primiparas in the so-called prophylactic sense to minimize the trauma to the fetus and the mother when the head has reached the perineum. It is significant that midforceps delivery is done 8 times more often in the cases of narrow pelvis

because of mid transverse arrest and persistent posterior positions. The incidence of midforceps in multiparas in the "narrow" group exceeds slightly that in primiparas in the "normal" group. The lessened frequency of midforceps delivery in multiparas of the "narrow" group is due to the relaxation of the levators, particularly the pubococcygeus bundle, allowing the head to descend more easily well down in the outlet segment. There was one fetal death in the normal group and three fetal deaths in the "narrow" group due to the delivery and apparently from intracranial hemorrhage. There were no maternal deaths.

Summary

A plea is made for more meticulous attention to outlet pelvimetry.

A comprehensive technique is outlined to cover all aspects of the pelvic outlet.

One thousand cases were reviewed to ascertain the incidence of narrow outlets, which amounted to 34 per cent.

Two hundred fifty patients with normal pelves were compared with 250 patients with narrow pelves as to frequency of failure of rotation and operative delivery.

There were eight times as many failures to rotate and midforceps deliveries in the narrow group.

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1180 BEACON STREET

THE VARIABILITY OF THE VASCULAR SUPPLY TO THE URETER

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THIS study of the arterial supply to the ureter was made because of the prevalence of injuries to the ureter in pelvic surgery and gynecologic complications to the ureter and kidney following pelvic intervention.

R. Brooke Bland[1] states that in 361 cases with injury the types of injuries were, listed in order of frequency: ligation, incision, excision, and necrosis due to vascular interference. Taussig,[25] writing on iliac lymphadenectomy with irradiation in the treatment of cancer of the cervix, points out: that the size of a gland did not determine whether it had metastasis or not; that irradiation of the cervix did not alter lymph node metastatic growth; that glands involved in order of frequency were iliac, obturator, ureteral, and sacral, and from these the second stage group, lumbar aortic, inguinal, and common iliac. Again in 1935 Taussig,[27] points out that radium implantation is not satisfactory and stressed the importance of complete lymphadenectomy, especially the parametrial, ureteral, obturator, and iliac groups. It will be readily seen then how, following a panhysterectomy where an attempt has been made to clean out the lymph node masses, it has often been noted that the ureter lies in the pelvis like a loose wire across a floor, and one can readily understand why the complications would involve the pelvic portion of the ureter. As radical surgery in the pelvic area becomes more and more important and a thorough cleansing of the pelvic glands more common, we note in the statistics that the first and most common complication is fistulas of ureteral origin, second, necrosis and atrophy of the kidney and the ureter involved, and, third, acute dilation of the ureter with retention.

Feeling, therefore, that damage to the vascular supply is the main factor in all complications following pelvic intervention, this study was undertaken in order to understand the variability of supply. I use the word "variability," for if one looks at our standard textbooks one comes to the conclusion that there is nothing actually definite. Gray's[6] gives no explanation of the arterial tree. Cunningham[2] refers to vessels that may come off in the abdominal portion from the renal or gonadic arteries, and in the pelvis from the vesicals or middle rectal arteries. Testut[26] gives the best description: the calices and pelvis are supplied by branches from the renal; the abdominal and iliac portions of the ureter by the renal, gonadic, aortic and or common, iliac; the pelvic portion by the internal iliac and by the vesical in the male or uterovaginal in the female. The intravesicular portion is also supplied by the arteries directly supplying the bladder.

Obviously the textbooks do not supply sufficient information for comprehensive understanding of the problems involved in radical surgery in this area.

The earliest complete study of ureteral blood supply was made by Sampson.[24]

There are three men whom Sampson quotes and these are Quain,[23] Morris and Disse,[3] the sum of whose material showed that, in the abdomen, branches to the ureter were from renal and spermatic, and in the pelvic portion were supplied by middle hemorrhoidal and inferior vesicle arteries.

He showed also a periureteral arterial plexus with branches from aorta, renal, gonadic, and iliac. This plexus anastomoses with vessels on the peritoneum and these peritoneal branches in turn help to supply the ureter.

Sampson also refers to a periureteral sheath in the abdomen. This requires a little imagination but a definite sheath is noted in the pelvis and close to the bladder we have a periureteral plexus and a reinforced muscular bundle. This was first noted by Waldeyer in 1892.

Any interference with this sheath, since it takes part origin from the ureter, will cause the ureter to be fixed in scar tissue. In his experimental work with dogs he showed this to be so, with the proximal part of the ureter becoming markedly dilated.

Following this excellent work a German by the name of Frommolt[4] in 1927 demonstrated the same thing as Sampson did, showing that the upper portion of the ureter, the middle, and the lower were generally supplied by the vessels closest to the ureter.

Nitch,[20] in his paper on transplant of the ureter in 1931, shows that if the vascular supply is high off the pelvic brim, the transplant will be good, but if the supply is low, near the bladder, it will be difficult to make a good transplant, and where the supply is very low and must be cut, success is questionable.

This is again confirmed by Harper[7] in 1942 in a very good paper on the blood supply of the human ureter. Meigs[14] quotes Neil who pointed out branches coming from the uterine artery. Meigs states that 12.3 per cent of the complications in his series of 65 Wertheim operations were ureteral fistulas.

Michaels[16] showed that the main supply is multiple, that this supply may be endangered in pelvic lymphadenectomy, that the branches from both ends though constant are small.

The consensus with regard to the periureteral arterial plexus is in agreement with the opinion of Sampson, who stated: "One should suppose that the destruction of the peri-ureteral arterial plexus for only a short distance would lead to necrosis of the ureters, for even if there should be a free anastomosis of the deep arteries of the ureter on account of their size and small numbers, one would not suppose that they would be capable of maintaining the nourishment of the ureter for any great distance."

Technique

Several methods were first tried for injecting the arterial tree, especially those developed by Lieb,[10] also that by Narat, Loef, and Narat,[19] but one after the other was discarded because: (1) cost and equipment were extensive; (2) a vessel would easily rupture; and (3) the injected material would fill the veins and make these indistinguishable from the arteries. The method finally used was extremely simple and entirely effective.

When an autopsy was required in the case of a newborn specimen, injection had to be made prior to the autopsy and with as little damage as possible. Permission was obtained to go into the thoracic cage, tie off the pulmonary hilum, and cut out the lung to get at the thoracic aorta. The aorta contained blood which was squeezed out. A glass cannula was then inserted into the aorta and tied in place with two sutures around the aorta. Next a slit was
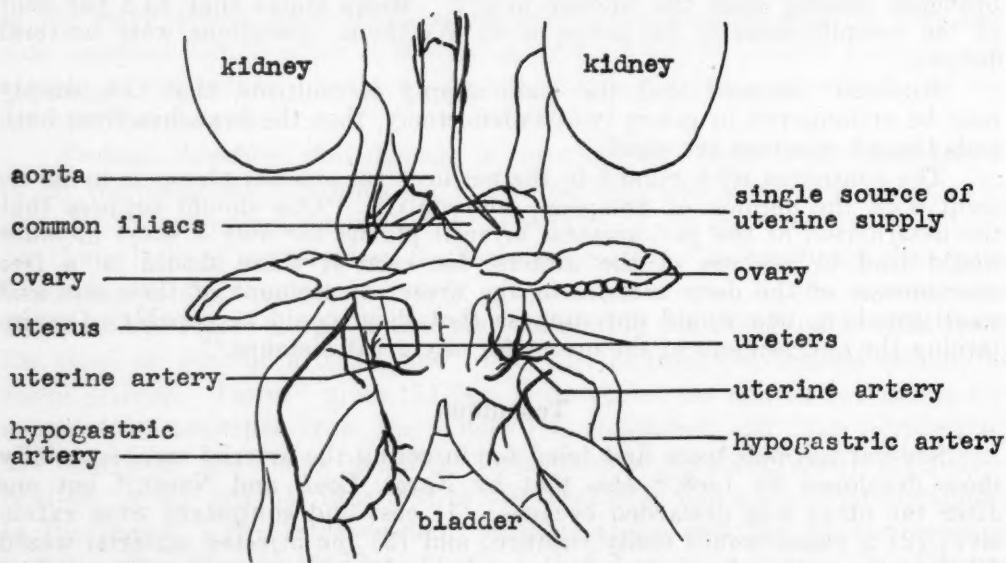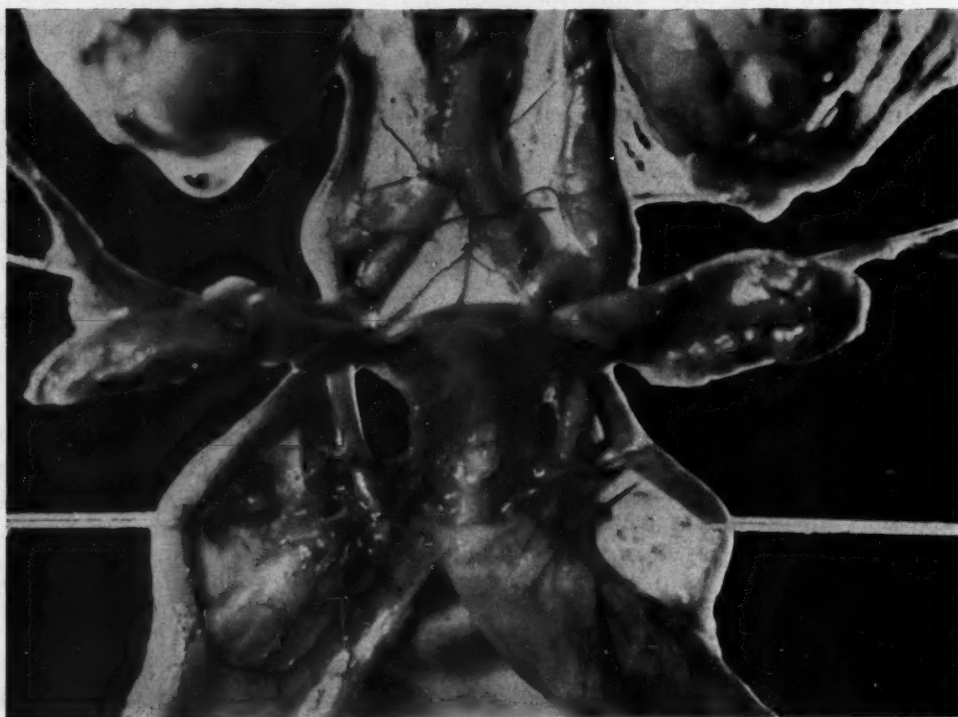
Fig. 1.—Female, fetus, anterior aspect. Note multiple branches from single source at bifurcation of aorta. Note uterine artery giving branches to ureter on lateral anterior aspect.

Fig. 2.—Male, newborn, anterior aspect. Note branches from internal iliac arteries. Note branches from internal iliac supplying terminal portion of ureter. Note anastomosis in peritoneum and in inferior mesenteric area and across bladder. Inferior mesenteric artery has been cut.

made in the abdominal wall so that a small loop of intestine was visible. Then with a rubber plunger syringe an injection of 20 to 40 c.c. of red pigmented latex was made into the aorta by way of the cannula. Pressure and amount of latex were judged by watching the vessels on the loop of intestine protruding from the slit in the abdominal wall. When these arteries were completely injected, the cannula was removed and the aorta tied off. When
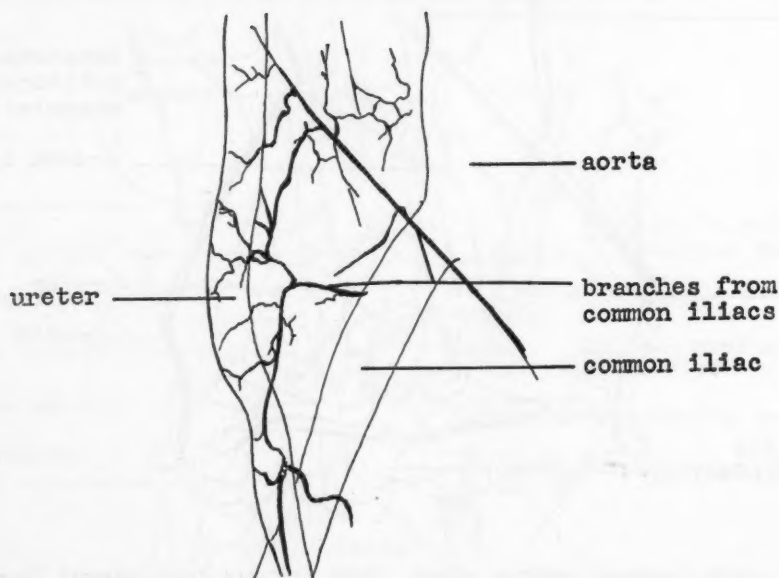
Fig. 3.—Female, fetus, anterior aspect. Note secondary branches lying loosely in areolar tissue with twiglike tertiaries more adherent to adventitia.

the Pathology Department was interested in the case, the particular organ of interest was dissected out, with care that, as much as possible, the retroperitoneal system of the posterior abdominal wall was left intact. The remainder of the specimen was then put in the refrigerator for 24 hours, in

Fig. 4.—Female, fetus, lateral anterior aspect. Note uterine artery and small adherent branches to ureter.

which time the latex had set. After eliminating the abdominal viscera, the urogenital system was removed en bloc, down from the diaphragm and with the terminal portion of the sigmoid and rectum. This portion of the bowel was later dissected out of the bloc. A rectangular frame was then made from a glass r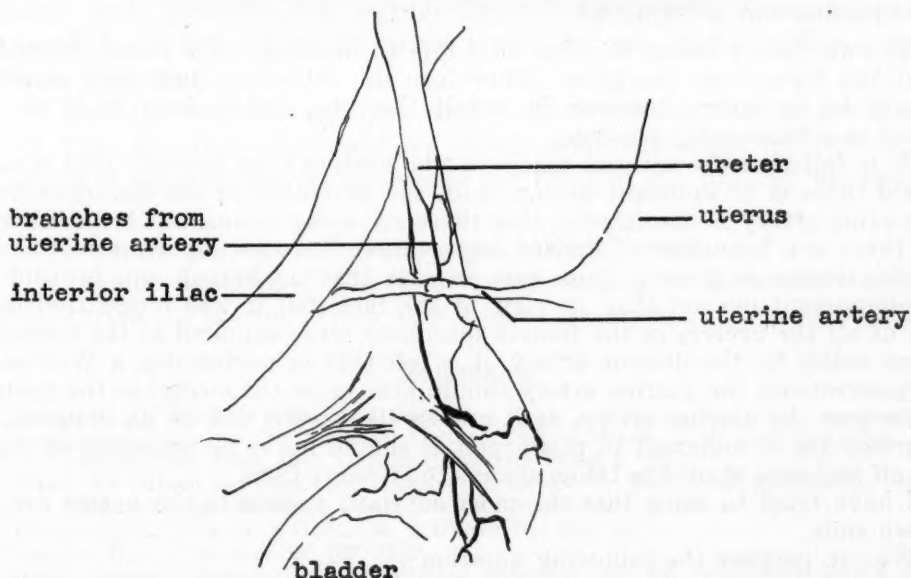od and the specimen sutured to it: through the kidneys laterally, the aorta above and the bladder below. The specimen was then fixed in a mild solution of formalin, or, in later specimens, Kaiserling I, in order to preserve the color.

This method was so entirely successful that it was used on all fetal and newborn specimens from the time its trial proved it effective.

Dissecting out of the vascular tree was done under water in a glass pie plate which, when placed on a Keleket x-ray view box, allowed light to penetrate from below. A magnifying glass with a light on a stand provided light from above, and the vessels were carefully traced to the ureters, genitals, bladder, and peritoneum covering these.

The adult specimens, five male and two female, were Department of Anatomy material and had already been impregnated with a preserving mixture of acid, aldehyde, and alcohol. These specimens were injected with a red lead mixture, but it was felt that all the vessels might not have been completely injected, and the possibility of error was such that dissection of adult specimens was soon discontinued.

Results

The arterial supply of the ureters of adults, newborn infants, and fetuses was studied with the following questions in mind:

1. Are any of the arteries constant, and if so what are their characteristics with regard to the ureteral segment supplied, position, and direction of vessels?

2. Are some of the vessels inconstant, and if so what are their characteristics with regard to length of ureteral segment supplied and size of vessel?

3. How closely is the vascular supply of the ureter associated with that of the peritoneum covering it?

It was always borne in mind that due to blockage of a vessel, injection might not have been complete. Therefore the following data may in some measure be in error; however, it is felt that the observations made are as correct as is reasonably possible.

It is felt that the arterial supply to the ureters is so variable that it may be said there is no constant supply, with the exception of the branches from the uterine artery in the female; that there are many inconstant branches and that there are branches of limited importance, but the importance of these branches varies so greatly from case to case that no branch can be said to be unimportant per se; that, in view of the fact that it was found that one-third of all the ureters in the female specimens were supplied at the terminal portion solely by the uterine artery, it is felt that in performing a Wertheim panhysterectomy the uterine artery should always be cut medial to the ureter, and because the uterine artery, as it crosses the ureter, and as its branches to the ureter are so adherent to this organ, it should never be necessary to strip them off and care should be taken always to preserve them.

I have tried to show that the most constant vessels to the ureter are at the two ends.

We can propose the following question:

Does the ureter always receive a supplementary supply from intermediate vessels?

We see that the newborn and fetus male ureters receive an average of 6.5 per cent and 4.5 per cent, respectively, and that of the newborn female 4.75 per cent and fetuses 4.25 per cent. Therefore, the answer to the afore-said question is yes.

Is there any constancy in this intermediate supply in regard to:

A. *Origin:* From aortic—40 to 45 per cent, from common or internal iliac —60 to 65 per cent, from gonadics—48 per cent, and from other sources we can say it was the exception rather than the rule.

B. *Magnitude or Distribution:* In the dissection of the newborn infants and fetuses, there were a total of 151 vessels dissected. These were classified large, medium, and small, the large being a vessel supplying more than one-half the length of the ureter, medium one supplying less than one-half, and small, a vessel supplying one-third or less of the ureter. The distribution of supply in dissection of newborn and fetal specimens showed that 78.1 per cent of the vessels supplied one-third or less the length of the ureter, 11.9 per cent less than one-half the length, and 10 per cent supplied more than one-half the length of the ureter.

Can this intermediate supply be sacrificed with safety?

Since the average ureter receives 4 to 5 vessels and since the average vessel supplies, in 78.1 per cent of the cases, one-third or less the length of the ureter, I believe one can sacrifice an intermediate vessel.

Can either of the terminal supplies be sacrificed?

Taking into account the figures previously mentioned and noting that in one-third of the female specimens dissected the only vessel supplying the ureter in the pelvis was the branch of the uterine, I would be skeptical of its sacrifice.

Conclusions

What precautionary steps must be taken by the surgeon?

Let us recall:

1. That the vascular supply to the ureter is from the medial side of the abdomen and, therefore, any retroperitoneal incision must be done lateral to the ureter; and that within the pelvis the lateral side, and therefore a medial incision, is advisable.

2. That the vascular supply is closely allied with that of the peritoneum.

3. That the ureteral vessels are closely adherent to the peritoneum.

4. That anastomosis occurs across the front of the bladder between the ureters.

5. That the uterine artery is the most constant vessel.

6. That in one-third of the cases the sole supply to the ureter within the pelvis is from the uterine artery as it crosses the ureter.

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ETIOLOGY OF PRE-ECLAMPSIA-ECLAMPSIA*

IV. Sodium Chloride Test for the Diagnosis of Pre-eclampsia†

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E DEMA has been one of the principal signs noted in pre-eclampsia-eclampsia and the cause has been attributed to a retention of sodium chloride. The retained salt was usually associated with a marked retention of water, resulting in visible edema. Several investigators have written of a so-called "dry retention" of sodium chloride in which there was no visible edema, but there would be an abnormal weight gain. For the past twenty years, edema has been associated with a retention of the sodium ion, although visible edema is extracellular, and the principal constituents of this fluid are sodium and chloride ions. No conclusive evidence is available to explain the high incidence of ankle edema in normal pregnant patients and the marked edema usually found in patients with pre-eclampsia-eclampsia.

We have been investigating the metabolism of sodium and chloride in normal pregnant and toxemic patients for many years. This study has shown great promise during the past six years since we began injecting sodium salts into normal and abnormal pregnant patients, and determining their elimination, as well as their toxic effect. We[1] reported that the intravenous injection of 1,000 ml. of a 2.5 per cent solution of sodium chloride in pre-eclamptic patients on two or more successive days caused marked increases in blood pressure, weight, and especially proteinuria. Some patients have developed symptoms suggestive of imminent eclampsia, and possibly one patient developed convulsions and coma (eclampsia) as a result of the injections. Intravenous injections of sodium lactate containing an equivalent amount of sodium ions caused no increase in severity of the pre-eclampsia if the patient was on a low-chloride diet. There is an increase of severity of symptoms and signs in the pre-eclamptic patient only when an adequate amount of the chloride ion is present. We[1] have also reported that certain patients who were admitted to the hospital with the clinical findings of pre-eclampsia were found to be able to eliminate the sodium ion in adequate amounts and concentrations to such a degree that the usual two intravenous injections of sodium chloride solution did not cause any increase in the signs and symptoms. The term "pseudo-pre-eclampsia" has been suggested for these patients. We stated that it was a waste of time to restrict the sodium intake in these patients. The oral administration of sodium salts has had results similar to those reported for the intravenous injection, but they are not as clear cut.[2]

Many injections of sodium chloride solution have been given to pre-eclamptic, hypertensive, and normal pregnant patients under controlled conditions in which the urine was collected periodically before and after the injection by retention catheter. The diagnosis of the clinical condition was made by the senior author without any knowledge of the chemical findings. The amount and concentration of sodium and chloride ions for varying periods after the injection have been studied by the statistician who did not see the patient. The results of this analysis, together with the diagnosis, form the basis of this report.

INTRAVENOUS INJECTION OF 2.5% Na Cl
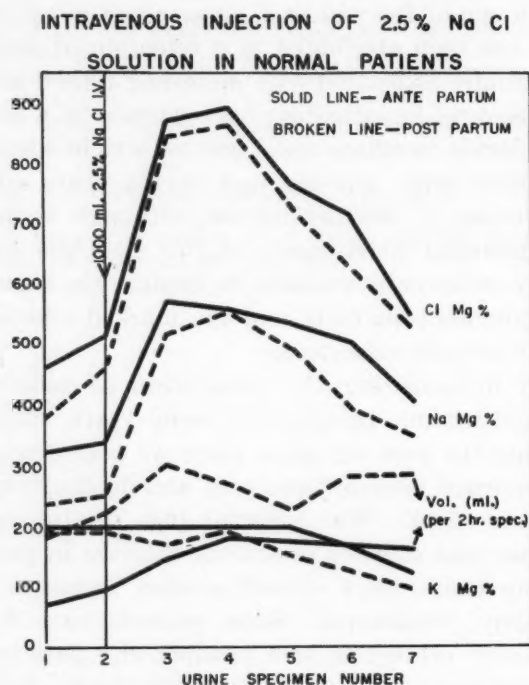SOLUTION IN NORMAL PATIENTS

Fig. 1.—Shows the effect of injecting 1,000 ml. of a 2.5 per cent solution of sodium chloride intravenously into normal pregnant patients. Each urine specimen number represents a two-hour collection of urine. In both antepartum and postpartum studies, there is a slight increase in the urine volume after the injection. There are marked increases in the urinary concentration of sodium and chloride ions after the injection, but very little change in the potassium concentration.

Almost all of the patients, especially during the antepartum period, were on a diet which contained less than 0.5 Gm. of sodium, 0.5 Gm. of chloride, and 1.0 Gm. of potassium. The urine specimens were collected every 24 hours. Beginning at 6:00 A.M., the morning of the test, the urines were collected every two hours for 12 hours, and then from 6 P.M. to 6 A.M. Numerous studies were made of the sodium and chloride excretion before and for varying periods of time after the injection which was usually given from 9:30 to 10:00 A.M. The changed rate of excretion in grams per hour as compared with the control period; the excretion in grams for varying periods of time after the injection; and, finally, the concentration of sodium and chloride ions for the various periods were all analyzed statistically. The conclusion was that the first two-

hour specimen immediately after the injection was the most valuable in indicating a difference between pre-eclamptic and hypertensive pregnant patients. The test as now modified involves the intravenous injection of 1,000 ml. of the 2.5 per cent solution of sodium chloride in a period of 30 to 40 minutes. A retention catheter is inserted before the injection and drained 15 minutes after the completion of the injection. Two one-hour specimens of urine are then collected and the concentration of sodium and chloride in each one is determined.

Fig. 1 shows the effect of the intravenous injection of sodium chloride in terms of the observed average values for a group of normal women. There is a moderate increase in urine volume and a precipitous jump in the concentration of sodium and chloride ions; potassium concentration does not appear to be markedly affected. By six hours after the injection (sample No. 5) the sodium and chloride ion concentrations have begun to drop, and in the last twelve hours of the test (sample No. 7, 8 to 20 hours after the injection) all values are approaching the levels observed before the test.

INTRAVENOUS INJECTION OF 2.5% NaCl SOLUTION
URINARY SODIUM CONCENTRATION - (mg %)

SOLID LINE - ANTE PARTUM
BROKEN LINE - POST PARTUM
■■■NORMAL
▲▲▲PRE - ECLAMPSIA
●●●HYPERTENSIVE DISEASE

URINE SPECIMEN NUMBER
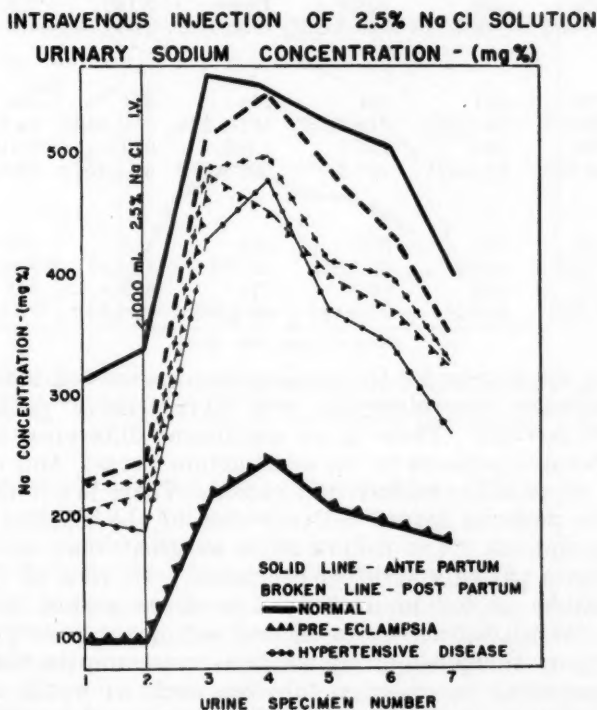
Fig. 2.—Injections of a 2.5 per cent sodium chloride solution were given intravenously, and the graph represents the mean concentration in milligrams of sodium. The pre-eclamptic patient shows a markedly decreased ability to concentrate sodium ions before delivery.

The means and ranges for the grams of sodium and chloride ions in the urine before and after the intravenous injection of 1,000 ml. of a 2.5 per cent solution of sodium chloride are given in Table I. These patients received 9.8 grams of sodium ions, and 15.2 grams of chloride ions, in addition to the diet which contained usually 0.5 gram of each. It is obvious that at the end of 20 hours after the injection, there was a positive balance for each ion in normal pregnant patients. Nonpregnant individuals also show a positive balance after a similar injection of sodium chloride, but not to the same degree. The pre-

eclamptic patient has a marked positive balance for the sodium ion, due to the decreased ability of the kidney to concentrate and the decreased urine volume. Since this retention in pre-eclamptic patients persists for days, it is obvious that a marked accumulation of sodium ions will take place. Undoubtedly, much of this sodium replaces intracellular potassium. Since intracellular sodium presumably does not combine with as much water as extracellular sodium, it is apparent why the degree of edema does not always parallel the amount of sodium ion retention or the severity of the condition.

TABLE I. SODIUM AND CHLORIDE ION CONTENT OF URINE BEFORE AND AFTER INJECTION OF SODIUM CHLORIDE (MILLIGRAMS)

ANTEPARTUM MEANS AND RANGE	LENGTH OF COLLECTION PERIOD						
	BEFORE INJECTION		AFTER INJECTION				
	2 HRS.	2 HRS.	2 HRS.	2 HRS.	2 HRS.	2 HRS.	12 HRS.
Normal Pregnancy.—							
Sodium	228	320	869	1,029	818	853	3,772
Observed range	36-520	118-728	385-1,891	140-1,891	341-1,770	341-1,311	624-4,920
Chloride	324	480	1,321	1,649	1,180	1,234	5,178
Observed range	95-685	122-1,118	560-3,052	785-3,052	460-2,340	460-1,552	1,077-8,201
Hypertensive Disease.—							
Sodium	149	271	821	776	621	694	2,291
Observed range	33-271	24-2,995	319-2,223	421-1,285	34-1,843	34-2,142	972-9,918
Chloride	206	398	1,277	1,182	939	1,019	3,360
Observed range	20-519	51-4,524	440-3,078	631-1,972	66-2,457	66-2,474	1,193-10,345
Pre-eclampsia.—							
Sodium	141	104	375	385	435	339	1,206
Observed range	6-248	4-592	45-1,855	22-770	30-1,077	9-853	115-3,689
Chloride	211	158	564	574	677	543	1,782
Observed range	2-410	4-971	93-3,115	60-1,395	45-1,743	27-1,273	300-5,464

Fig. 2 shows the graphs for the mean concentrations of sodium in the urine for normal pregnant, pre-eclamptic, and hypertensive patients, both ante partum and post partum. There is no significant difference for normal pregnant and hypertensive patients in the antepartum period, and no difference for any of the three types in the postpartum period. There is a noticeable difference for pre-eclamptic patients before delivery due to the marked decrease in the concentration of sodium. The difference is so great that we think it can be used to differentiate patients with pre-eclampsia. In view of the fact that the average daily intake of sodium is 3 to 6 or more grams, and the pregnant patient has this diminished ability to excrete sodium, it is surprising that there is not a much higher incidence of edema and pre-eclampsia than exists. Obviously, any derangement in water metabolism such as would occur on a cool day (decreased intake) or on a very hot day (increased sweating) would very definitely diminish sodium excretion. If these alterations were repeated frequently enough or of long enough duration, there would be a very marked retention of sodium within the body with its resultant disturbance in the sodium and potassium balance, especially within the cell.

Fig. 3 shows the concentration of urinary chloride. The curves are very similar to those for sodium concentration and, in general, the chloride determination can be used instead of the sodium for determining whether or not the patient has pre-eclampsia. The chloride intake must be normal.

Fig. 4 shows the urine volume after an intravenous injection of 2.5 per cent sodium chloride solution. In a previous report, we[3] stated that the pregnant patient had a delayed elimination of water which was greatly intensified in

the patient with pre-eclampsia. The curves and the water clearance test indicated some derangement of the adrenal cortex. The grouping of the antepartum and postpartum curves after the injection is quite significant, indicating the effect of pregnancy on the urine volume after the intravenous injection. It is quite apparent that the change in the urine volume by the seventh to twelfth day post partum indicates that the removal of the pregnancy has had a very definite effect on whatever secretions affect urine volume.
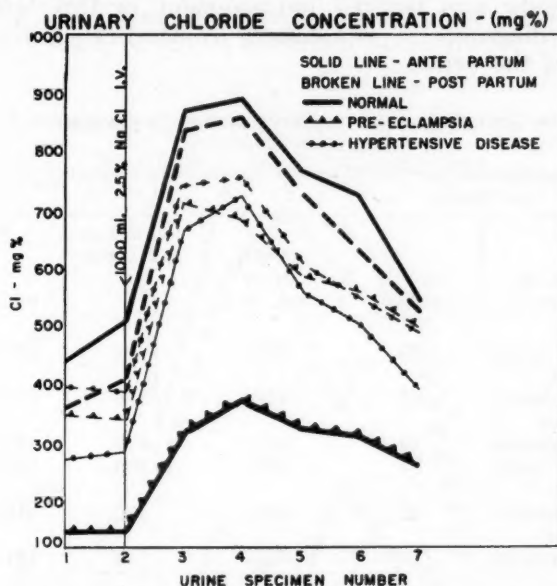

Fig. 3.—Injections of a 2.5 per cent sodium chloride solution were given intravenously, and the graph represents the mean concentration in milligrams of chloride. The pre-eclamptic patient shows a markedly decreased ability to concentrate chloride ions before delivery.

The potassium excretion has also been studied. There is a grouping of antepartum and postpartum values but it is not as marked as for the urine volume. There is no characteristic curve produced for pre-eclampsia or hypertensive disease as distinguished from that of normal pregnant patients.

The data in Table II show the concentration of sodium, A, and chloride ion, B, in the urine collected during the first two-hour period following the saline injection. The differences between the three groups in terms of average response are striking. The differences between each pair of means for both sodium and chloride ion reach or far surpass a significance level of $P = 0.001$. Even the standard error ranges show little or no overlap. In mean value the tests distinguish well between normal pregnant women, patients with essential hypertension, and those with pre-eclampsia.

The data in Table III are used for differentiating pre-eclampsia from hypertensive disease and "pseudo-pre-eclampsia." They were derived by adjusting the standard error ranges of Table II to eliminate overlap and to cover the entire range of possible concentration values.

In patients in whom the clinical diagnosis was hypertensive disease in pregnancy, the test assigned the case to the wrong toxemia in 21 per cent. Where the clinical diagnosis was pre-eclampsia, the test assigned the case to the wrong toxemia in 10 per cent.

Eleven patients with "pseudo-pre-eclampsia" were able to concentrate sodium and chloride in the range greater than that of pre-eclampsia. Furthermore, these patients had less impairment of water elimination; thus injected sodium ions were eliminated either by increased concentration, augmented urine volume, or by both.

The data in Fig. 5 show the concentrations of sodium and chloride before and after delivery in the various conditions mentioned.

Some pregnant patients with chronic glomerulonephritis show antepartum sodium values which are in the pre-eclamptic range. However, they have nearly always failed to show any marked improvement in this test after delivery. Furthermore, the diagnosis is established by studies of the renal function and examination of the urine.

TABLE II. SODIUM ION CONCENTRATION IN URINE AFTER INTRAVENOUS INJECTION OF SODIUM CHLORIDE SOLUTION

A

TIME OF TEST	TYPE OF CASE	NO. OF CASES	SODIUM MEAN (MG. %)	STANDARD DEVIATION + −	RANGE (MG. %)	
					OBSERVED	FROM STANDARD ERROR*
Ante partum	Normal pregnancy	18	563	92	432-760	497-629
Ante partum	Hypertensive disease	28	450	120	213-610	381-519
Ante partum	Pre-eclampsia	20	233	149	16-530	131-335
Post partum	Normal pregnancy	33	539	109	210-685	485-593
Post partum	Hypertensive disease	42	501	105	210-700	450-552
Post partum	Pre-eclampsia	29	495	118	124-705	429-561

B

CHLORIDE ION CONCENTRATION

TIME OF TEST	TYPE OF CASE	NO. OF CASES	CHLORIDE MEAN (MG. %)	STANDARD DEVIATION + −	RANGE (MG. %)	
					OBSERVED	FROM STANDARD ERROR*
Ante partum	Normal pregnancy	15	834	92	630-1,110	735-933
Ante partum	Hypertensive disease	22	669	120	309- 925	579-759
Ante partum	Pre-eclampsia	17	363	149	73- 890	204-522
Post partum	Normal pregnancy	28	866	100	455-1,170	794-938
Post partum	Hypertensive disease	34	755	107	302-1,022	674-836
Post partum	Pre-eclampsia	24	725	117	295-1,060	623-827

*The range derived from the standard error is obtained by adding and subtracting 3 times the standard error from the observed mean.

TABLE III. VALUES FOR URINARY SODIUM AND CHLORIDE ION CONCENTRATIONS USED IN DIFFERENTIAL DIAGNOSIS

CASE ASSIGNED TO	SODIUM RANGE		CHLORIDE RANGE	
	MG. %	MEQ. PER LITER	MG. %	MEQ. PER LITER
Pre-eclampsia, up to	332	144	518	146
Hypertensive disease	332-506	144-220	518-768	146-217
Normal pregnancy, over	506	220	768	217

Comment

Pre-eclampsia-eclampsia is distinguished from hypertensive disease and acute or chronic kidney disease in pregnancy by the history, clinical and laboratory findings. However, if patients are not seen until the condition is present, the differential diagnosis is frequently difficult.

Dieckmann in 1936[4] and 1941[5] reported that the patient with true pre-eclampsia-eclampsia has a marked hemodilution coincidental with clinical improvement. If this occurs before delivery, it is of material aid in establishing the proper diagnosis. However, if it occurs after delivery, the hemodilution may be due to the blood loss, the toxemic condition, or to both. If the blood loss was less than 300 ml. of blood, abnormal hemodilution signifies pre-eclampsia-eclampsia.
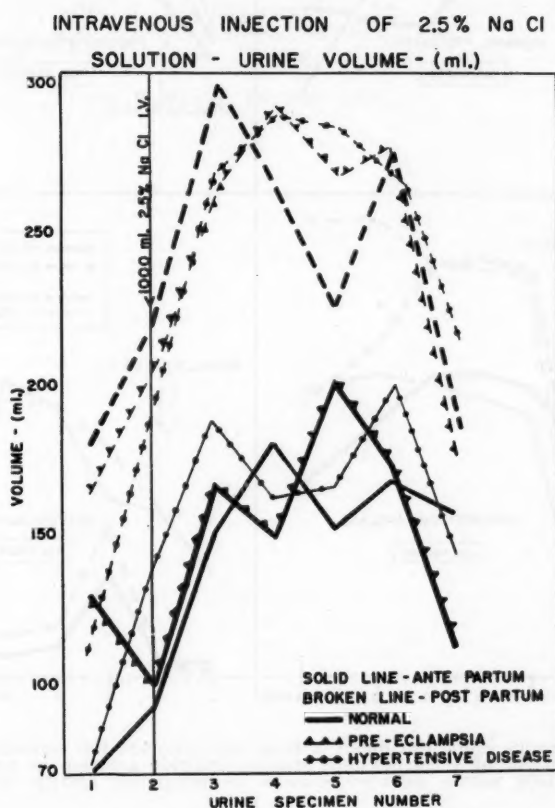

Fig. 4.—The graph shows that pregnancy in normal pregnant, pre-eclamptic, and hypertensive patients causes an impaired elimination of water, as compared with that of the same patients under the same test conditions during the puerperium.

Chesley[6] has reported that the ratio of the uric acid clearance to urea clearance is of value in the differential diagnosis. In an unreported study we have not been able to confirm this statement.

The determination of the ability of the patient to concentrate sodium or chloride ions in the urine after a test dose seems to offer an excellent means of differentiating patients with pre-eclampsia from patients with vascular or renal disease in pregnancy, as well as from patients with "pseudo-pre-eclampsia."

In this report, we have deliberately omitted all discussion about water, sodium and chloride metabolism, the adrenal and posterior pituitary gland
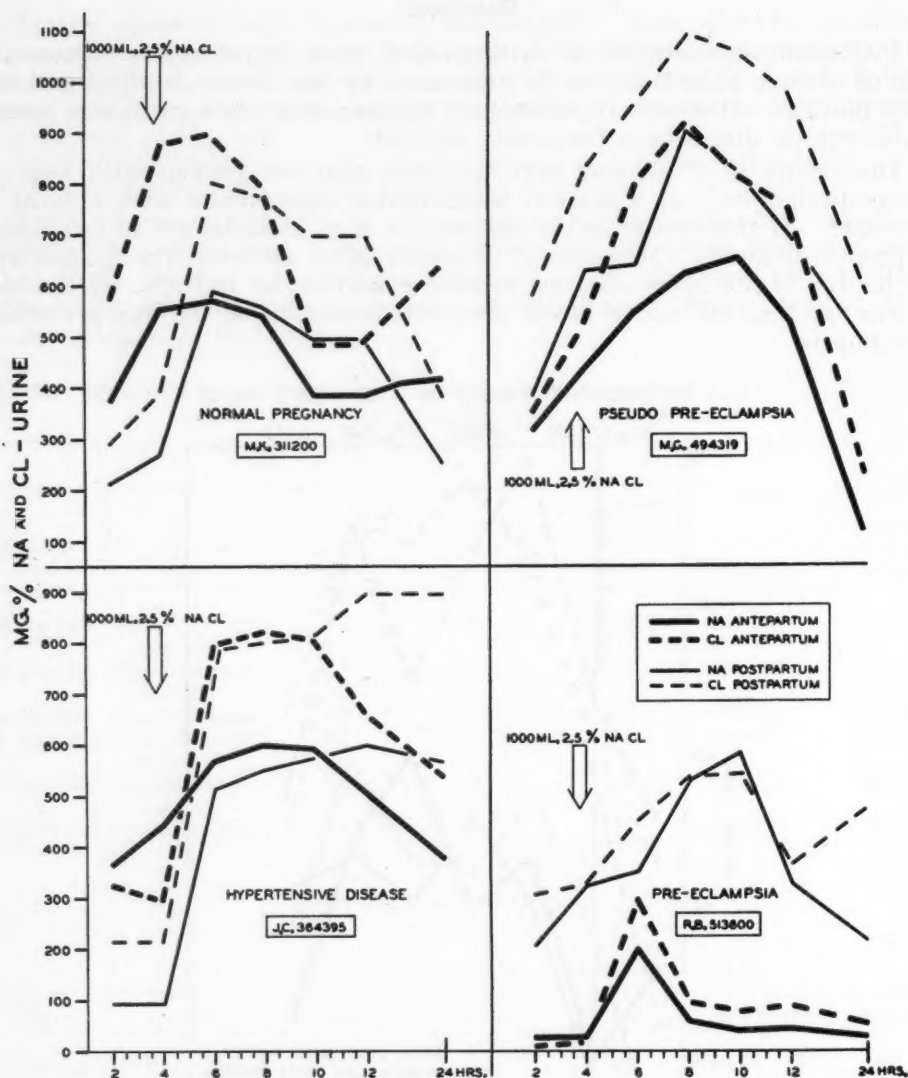
Fig. 5.—These graphs show the mean sodium and chloride ion concentrations in the urine after intravenous injections of a 2.5 per cent sodium chloride solution in four different patients. The pre-eclamptic patient before delivery showed a diminished ability to concentrate sodium and chloride.

hormones, and the vascular renal physiology. We hope that studies still in progress will aid us in a satisfactory explanation of the changes reported.

Conclusions

Pregnant patients with pre-eclampsia-eclampsia are not able satisfactorily to concentrate sodium or chloride ions in the urine. By the seventh day after delivery and earlier in some pre-eclamptic patients, this diminished ability to concentrate has disappeared.

As a result of the inability to concentrate sodium or chloride after a test dose, together with the decreased ability to excrete water in pre-eclamptic-

eclamptic patients, there is a delayed elimination of sodium and chloride after a test dose of sodium chloride.

The low concentration of sodium and chloride in the antepartum urine after a test injection of sodium chloride solution is characteristic of patients with pre-eclampsia-eclampsia.

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EDUCATION FOR CHILDBIRTH IN PRIVATE PRACTICE

450 Consecutive Cases

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THESE statistics are being published to show the scientific results of education or training for childbirth in private practice. The training period began only two months prior to the time we began recording statistics, which means that the first patients had very little training. The 450 cases include all consecutive deliveries, except those of less than 28 weeks' gestation, from Jan. 1, 1951, to Nov. 1, 1951. Even the 10 patients we knew would require repeat sections were included because we have learned that these patients have a more comfortable pregnancy by taking part in the exercises and they approach their surgery with a better emotional attitude.

We began our program first by a careful study of Grantly Dick Read's book, *Childbirth Without Fear*,[1] and then by sending a registered nurse (Miss Bell) to Grace Hospital, New Haven, for a three months' course in the technique. The nurse gives four classes on exercises, education, and relaxation. These classes are two hours in length. From 10 to 12 expectant mothers are present in each of these classes. We give two lectures to the mothers and fathers, one on prenatal care and delivery, and the other on neonatal care.

Our program differs from that at Yale[2] in that one nurse has given all the class work and all the babies are delivered by us personally. In fact, 90 per cent of the deliveries were by one of us (H. L. M.) and 10 per cent by the other (F. E. F.). Also, all the support during labor was given by the same nurse who gave the class instruction or by one of us, and all prenatal visits were conducted by the two of us. The reason we mention this is because we feel that this personal attention has given the patients a greater feeling of security than where many different individuals may be caring for the same patient.

We have learned more about how to make the program more successful as we have taken care of more cases. We ask most patients in what way they think we can improve and have followed many suggestions. We learned rather early, for example, that too much Demerol has a tendency to cause confusion and lack of cooperation, while a smaller dose causes relaxation and perfect cooperation. A former nurse whose case we considered a "failure" brought this to our attention. As a result, at the present time we seldom use more than 50 mg. of Demerol and many times we feel that this is not necessary.

In the first three months the primiparas averaged 11 hours in labor. Now they average a little over nine hours which includes those early cases that averaged 11 hours. This we feel signifies that the method has improved during the past few months.

In this paper we have not tried to evaluate the emotional and psychological improvement in the patients, nor have we tried to measure the amount of pain or discomfort they have had. We feel that this cannot be expressed without causing criticism by those not in favor of the method, and we also feel there is no way of measuring pain objectively. We do feel that the response of the patients has been more than satisfactory because in a private practice the amount of obstetrics we are continuing to do shows that these patients must have been satisfied. Most of them say they would not want to have a baby any other way, and now a few of the early ones are returning for care in subsequent pregnancies. We have no reason to believe that many are going to another obstetrician. Perhaps early in the program some did hesitate to come to us because of the common misconception that "natural childbirth" means no analgesia and no anesthesia.

TABLE I. LENGTH OF LABOR IN ENTIRE SERIES

Total number of deliveries				450
Multiparas		285		
Primiparas		165		
Average first stage	6 hours	48	minutes	
Average second stage		27.66	minutes	
Average third stage		5.63	minutes	
Total average hours in labor	7 hours	21	minutes	

Table I shows the total number of cases and the average number of hours in labor. At a glance one can see the reduction in hours in labor in this method. According to Williams,[3] the average number of hours for a primipara is 16 to 18, and for multiparas about 6 hours less. In this series the average for primiparas was nine hours, 27 minutes, and for multiparas 5 hours, 26 minutes.

We have designated the onset of labor as the time when the patients said they began having regular contractions. In some cases of multiparas, where we felt labor began before regular contractions, we considered labor starting when irregular contractions began, providing the patient did go on into active labor. For example, several multiparas had irregular contractions for four to five hours, and then after an enema had regular contractions for about an hour before delivery. In these cases we considered labor to be from the beginning of the irregular contractions. In other words, we have kept our statistics in a manner to give an accurate time interval for each stage of labor, and have not let our enthusiasm for the method deter us from accurate statistics.

As anyone knows who has tried to keep these statistics, it is occasionally difficult to decide when labor did actually begin. In any case of doubt we have used the longer time interval rather than the shorter.

There was a surprisingly high percentage of spontaneous deliveries (Table II). This we feel is due to the instruction and relaxation, because these patients know what is going on throughout their labor, and know what to do at the various stages.

TABLE II. TYPE OF DELIVERY IN ENTIRE SERIES

TYPE OF DELIVERY	NO.	PER CENT
Spontaneous	426	95.12
Forceps (low)	5	1.11
Breech extractions	2	
Sections	17	3.77

Table III shows the number who attended lectures and classes. The number now attending classes has increased so that it is near 100 per cent. The reason many do not attend the lectures is because of the husbands' working hours.

TABLE III.   PERCENTAGE OF PATIENTS WHO ATTENDED CLASSES AND LECTURES

	NO.	PER CENT
Attended classes	390	86.66
Attended lectures	297	66.00

However, all patients, whether they attended classes or not, did receive support during labor, and we feel that this support by trained personnel aids them greatly even though there has been no previous instruction.

We have divided the primiparas and multiparas into two groups for all the rest of the statistics.

Table IV shows the type of delivery in the 285 multiparas.

TABLE IV.   TYPE OF DELIVERY IN 285 MULTIPARAS

	NO.	PER CENT
Spontaneous	273	95.80
Sections	12	4.20
Forceps	0	0

The sections will be explained below. There were no forceps deliveries although many of these had had forceps with previous pregnancies.

The short duration of the second stage indicates (Table V) also that forceps certainly were not indicated to relieve pressure of the baby's head on the perineum.

TABLE V.   LENGTH OF LABOR IN 285 MULTIPARAS

	HOURS	MINUTES
First stage	5	6
Second stage		13.95
Third stage		5.83
Total hours in labor	5	26

Included in the length of the third stage are those cases in which a manual removal of the placenta was necessary, after a wait of approximately an hour for it to separate.

Table VI shows the number and percentage of the various positions. The only significant fact in this observation is that there is a smaller percentage of posteriors than is usually seen. We attribute this to the relaxation of the patient because we have seen several posteriors rotate near the end of labor

TABLE VI. PRESENTATIONS IN MULTIPARAS, 275 INFANTS (2 SETS OF TWINS) EXCLUDING THE 12 SECTIONS

POSITIONS	NO.	PER CENT
Left occipitoanterior	183	66.54
Right occipitoanterior	67	24.36
Right occipitoposterior	7	2.54
Left occipitoposterior	3	1.09
Footling breech	3	1.09
Frank breech	10	3.60
Transverse:		
Shoulder	1	0.36
Hand	1	0.36

and deliver in the anterior position. We considered them to be in the anterior position when the head was born in the anterior position.

Table VII shows the amount of medication given to the 273 multiparas who delivered spontaneously.

TABLE VII. MEDICATION IN 273 MULTIPARAS

	NO.	PER CENT
None	66	24.13
Demerol (125 mg. or less)	200	73.26
Demerol (over 125 mg.)	7	2.64

In 143 of these who received Demerol, only 50 mg. were given. This means that 84 per cent received 50 mg. or less. At times these patients had to be urged to take even the 50 mg. of Demerol.

Table VIII shows the amount of anesthesia given to the multiparas.

The anesthetic agent used was nitrous oxide and oxygen. We usually use an 80 per cent nitrous to 20 per cent oxygen mixture.

The 233 who received whiffs were fully conscious at all times and heard the baby's first cry.

TABLE VIII. ANESTHESIA IN 273 MULTIPARAS

	NO.	PER CENT
None	28	10.25
Whiffs	233	85.25
Partial anesthesia	11	4.02
Complete	1	0.36

Partial anesthesia was considered present each time the mother was unconscious even for a moment. These were the patients who asked to be asleep or those who had breech deliveries.

The one complete anesthetic was given to one of the patients with transverse presentations in which version and extraction were done.

Table IX shows the percentage of episiotomies and lacerations. There is nothing significant here because we feel that an episiotomy should be done wherever it will save time for the mother or to prevent a deep tear.

TABLE IX. EPISIOTOMIES IN 273 MULTIPARAS

	NO.	PER CENT
Episiotomy	118	43.22
No episiotomy and no tear	117	42.85
First-degree laceration	35	12.45
Second-degree laceration	3	1.09

However, it is worth while to note that in 42 per cent no episiotomy was necessary in spite of the short duration of the second stage. A local infiltration of 1 per cent Novocain was used for all repairs.

Table X shows the type of delivery in the 165 primiparas:

TABLE X. DELIVERY IN 165 PRIMIPARAS

	NO.	PER CENT
Spontaneous	155	93.33
Section	5	3.33
Forceps (low)	5	3.33

In Table XI the number of hours in labor for the 165 primiparas is presented.

TABLE XI. LENGTH OF LABOR IN 165 PRIMIPARAS

	HOURS	MINUTES
First stage	8	30
Second stage		41.37
Third stage		5.43
Total labor	9	27

Again the short duration of the second stage is important in view of the fact that forceps were used in only 3.3 per cent of the cases.

Table XII shows the positions, and, as in the multiparas, there is nothing significant, except that there were probably fewer posteriors than are ordinarily seen.

TABLE XII. PRESENTATIONS IN 160 PRIMIPARAS

POSITIONS	NO.	PER CENT
Left occipitoanterior	103	64.37
Right occipitoanterior	48	30.00
Left occipitoposterior	4	2.50
Right occipitoposterior	2	1.25
Frank breech	2	1.25
Footling breech	1	.62

In Table XIII the medication for the 160 primiparas delivered vaginally is presented.

TABLE XIII. MEDICATION IN 160 PRIMIPARAS

	NO.	PER CENT
None	8	5.00
Demerol (125 mg. or less)	114	71.25
Demerol (over 125 mg.)	38	23.75

In 36 per cent of those receiving Demerol, only 50 mg. were given. We feel that if 50 mg. of Demerol are given just prior to the transitional stage, it will help the patient, although at the time it is given she may think it rather unnecessary.

Table XIV shows the amount of anesthesia used in the primiparas. It is interesting to note that almost twice as many primiparas go without anesthesia as multiparas. We feel this is partly due to the fact that multiparas have had anesthesia in previous deliveries and consider it a necessity. However, we feel, too, that a few whiffs of gas are beneficial—if for no other reason than to prevent the patient from saying that she received nothing during her delivery. This factor has to be considered in a private practice.

TABLE XIV. ANESTHESIA IN 160 PRIMIPARAS

	NO.	PER CENT
None	32	20.00
Whiffs	117	73.12
Partial	4	2.50
Complete	7	4.37

Again nitrous oxide and oxygen in 80:20 mixture were used. Many of those receiving gas had a very negligible amount and would turn their faces away from the mask when they felt themselves becoming narcotized. In most cases the amount of gas given was ascertained by the patient's desire. In a few cases we have insisted on partial or complete anesthesia.

The amount of nitrous oxide used in the 450 cases was less than 7 size E tanks. This does not include the anesthesia given in the sections, nor in the

8 cases where complete anesthesia was used. This is an average of about 1 size E tank of nitrous oxide to 61 patients.

The episiotomies done in the primiparas reached a much higher percentage than in the multiparas (Table XV). We do not feel that the second stage should ever be prolonged just to eliminate an episiotomy.

TABLE XV. EPISIOTOMIES AND LACERATION IN 160 PRIMIPARAS

	NO.	PER CENT
None	10	6.25
Episiotomy	143	89.37
First-degree laceration	6	3.75
Second-degree laceration	1	0.62

One of the most satisfying results in this method is the morbidity or lack of morbidity in the mother. There were no maternal deaths, although this is not significant in this small number of cases (Table XVI). All mothers left the hospital in 7 days or less. Two patients had a uterine inertia following delivery, and a uterine pack was inserted for a few hours. Neither of these had to have transfusions. One patient had a submucous fibroid, and she continued to have excessive bleeding. Three weeks following delivery, a curettage was done, which failed to stop the bleeding. A hysterectomy subsequently had to be performed.

TABLE XVI. MORBIDITY

All patients home in 7 days	
Hemorrhage:	
Patients who required packing	2
Transfusions	2

Transfusions were given to the two patients who had placenta previa and abruptio placentae.

There were no cases in which pelvic or bladder infection could be demonstrated.

There were no intrapartal deaths. In the three stillbirths listed in Table XVII the fetus was dead prior to hospital entrance.

The neonatal deaths (Table XVII) also cannot be attributed to any method. Autopsies were performed in all cases. Three infant deaths within the first 7 days of life were due to marked congenital defects of the heart.

TABLE XVII. STILLBIRTHS AND NEONATAL DEATHS

	NO.	PER CENT
Stillbirths	3	0.66
Neonatal deaths	4	0.88
3 Congenital heart disease		
1 Erythroblastosis		

TABLE XVIII. CESAREAN SECTIONS EXPLAINED

Multiparas	12
Repeat sections	10
Abruptio placentae	1
Placenta previa	1
Primiparas	5
Toxemia	1
Arthritis	1
Fetal heart tones irregular and weak	1
Prolonged labor with no progress	1
Small pelvis (disproportion)	1

The erythroblastotic baby lived only a few minutes and was markedly hydropic when born, weighing over 7 pounds, although the mother was only in her eighth lunar month of pregnancy.

We feel that our percentage of cesarean sections in this series is quite high (3.77 per cent), due to the large number of repeat sections (Table XVIII). We never try to deliver a patient vaginally who has had a previous section, no matter what caused her to have the original section.

The section done in the primipara in whom the fetal heart tones became irregular and weak might possibly have not been needed, but in this case the couple had been married several years, and the mother had had two spontaneous abortions. At the time of the section, she had been in labor about 14 hours and the cervix was dilated only 4 cm. All the babies from the sections are alive and well.

Summary and Conclusions

1. The total number of hours in labor is greatly reduced, especially in primiparas.

2. Morbidity is greatly lessened in mothers and babies. The mothers feel better during pregnancy, and especially following delivery. The babies rarely show anoxia or atelectasis. Most babies begin to cry immediately after delivery. None of the babies required resuscitation.

3. Deliveries are less complicated, which adds to the safety of mother and baby. We feel that the safety factor is one of the outstanding points to be considered in any method used.

4. Average loss of blood is much less, although uterine inertia may still occur as it did in two of these cases.

5. No real attempt was made to evaluate the amount of pain or discomfort that these patients had. However, it is safe to say that they must have had very little in the majority of cases as evidenced by their enthusiasm in recommending the method to other expectant mothers.

6. Support during labor by properly trained nurses or doctors makes the program more successful. We feel that a trained person should give support from the time active labor begins until the baby is delivered. We have tried never to leave these patients alone. The nurse is with almost all patients from the time they are in active labor. We feel also that it is beneficial for the obstetrician to put in an appearance early in the patient's labor, and to be present especially during the transitional stage. We never leave the hospital when a multipara is in active labor.

7. We believe that probably the few people who are criticizing the method have not given it a fair trial, or else may have had a deflation of the ego when they saw how successfully a patient could accomplish, with proper preliminary training, what a physician has been trained for years to do with all sorts of specialized drugs and instruments.

If these few critics would take the time to train a few patients rather than to quibble[4] over the term "natural childbirth" and whether a patient is "hypnotized" or "relaxed," I believe they would find their time well spent and would enjoy the results.

We, also, do not especially favor the term "natural childbirth" and its implications, but we do approve of the satisfactory results we are obtaining no matter what term may be used to describe the method.

Like others, we feel that having a baby is a muscular effort. In fact, the second stage is a strenuous muscular effort.[5] However, for years, doctors have delivered millions of babies with no muscular preparation in the mother, though we would not expect an athlete to take part in a tournament without training in his particular field.

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1114 FIRST AVENUE, N.E.

PRIMARY ADENOCARCINOMA OF THE CERVIX*

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A DENOCARCINOMA of the cervix is not a common neoplasm; it frequently
is confused clinically with primary squamous-cell carcinoma of the cervix;
the treatment of choice has not been established; hence data on the outcome
of the disease vary greatly from author to author.

In a comprehensive review of the literature, relatively few articles were
found which covered both the clinical and the pathologic aspects of this tumor.
In 697 of the 15, 476 collected cases of cancer of the cervix (4.5 per cent) the
tumors were adenocarcinomas. The ratio of primary adenocarcinomas of the
cervix to all carcinomas of the cervix, as reported in the reviewed articles,
ranged from a low of 0.42 per cent to a high of 11.7 per cent (Table I).

TABLE I. INCIDENCE OF ADENOCARCINOMA OF THE CERVIX AS REPORTED IN THE LITERATURE

		CANCER OF THE CERVIX		
			ADENOCARCINOMA	
AUTHOR	YEAR	ALL CASES	CASES	PER CENT
Baldwin	1931	722	55	7.6
Bartlett and Smith	1931	560	66	11.7
Bowing and Fricke	1938	1,491	53	3.5
Chambers	1935	678	50	7.3
Dargent and Bonniot	1946	1,294	46	3.6
Döderlein	1931	362	16	4.4
Fluhmann	1927	110	6	5.4
Given	1947	212	17	7.9
Haupt (Norris)	1933	450	29	6.4
Healy	1931	1,574	43	2.7
Hoge	1941	237	8	3.0
Kamniker	1932	245	23	9.3
Keller	1930	463	9	2.1
Johnson and Tyrone	1934	268	17	6.5
Lynch	1934	375	18	4.8
Maliphant	1933	236	10	4.2
Martzloff	1923	387	21	5.4
McNamara	1930	294	3	1.02
Nilsson	1933	909	26	2.8
Norris	1936	508	43	8.45
Pack and Le Fevre	1930	2,134	9	0.42
Peterson	1919	406	37	9.1
Ross, J. W.	1922	277	28	10.1
Ross, R. A.	1933	81	4	4.9
Smythe	1937	357	2	0.56
Taylor and Peightal	1924	201	9	4.47
von Franque (Norris)	1930	120	8	6.66
von Graff	1934	263	19	7.2
Ward	1933	262	22	8.35
Total		15,476	697	4.5

Material

We have made a clinical and pathologic study of 164 cases of primary adenocarcinoma of the cervix. In 35 of these cases treatment consisted primarily of surgical removal of the uterus, and in 129 cases treatment consisted of irradiation with radium or roentgen rays, or with both.

Analysis of Data

The average age of the patients in our 164 cases was 50.1 years. In the surgically treated group the average age was 46.9 years, the oldest being 68 and youngest 24. In the group treated primarily by irradiation, the average age was 51 years and the range was from 13 to 78 years.

The frequency of occurrence of the various symptoms is shown in Table II. The term "bleeding" is used here to cover all forms of atypical vaginal bleeding; this was frequently described by the patient as just "bleeding," or "spotting," "vaginal bleeding," "irregular bleeding," or "bleeding between periods." The term "pain" here refers to abdominal, back, or pelvic pain.

TABLE II. INCIDENCE OF VARIOUS SYMPTOMS IN 164 CASES OF ADENOCARCINOMA OF THE CERVIX

SYMPTOM	CASES	PER CENT (OF 164)
Bleeding (atypical forms)	145	88.5
Leukorrhea	102	62.2
Frequency, dysuria, or both	18	10.9
Pain	59	35.9

All but 11 of the 164 cases were classified according to the stage of anatomic involvement by the neoplasm, as defined by the League of Nations; in the 11 unclassified cases the stage of involvement was unknown. The average stage of involvement was found to be 2.6 (Table III).

TABLE III. DISTRIBUTION OF 164 CASES OF ADENOCARCINOMA OF THE CERVIX ACCORDING TO STAGE OF ANATOMIC INVOLVEMENT

STAGE	CASES	PER CENT (OF 164)
1	26	15.8
2	37	22.6
3	61	37.2
4	29	17.7
Unknown	11	6.7

TABLE IV. DISTRIBUTION, ACCORDING TO STAGE OF ANATOMIC INVOLVEMENT, OF 59 CASES OF ADENOCARCINOMA OF THE CERVIX IN WHICH PAIN WAS A PRESENTING SYMPTOM

STAGE	CASES	PER CENT (OF 59)
1	2	3.6
2	9	15.2
3	26	44.1
4	18	30.5
Unknown	4	6.7

Of the 59 patients who presented pain as a symptom, the average stage of anatomic involvement was 3.1. The distribution of these patients according to

stage of anatomic involvement is given in Table IV. From the table it is evident that in approximately three-fourths of these cases, the involvement was classified as being in Stage 3 or Stage 4.

We classified these tumors, on the basis of gross characteristics, into five groups, using the self-explanatory descriptive terms as listed in Table V.

TABLE V. CLASSIFICATION OF 164 CASES OF ADENOCARCINOMA OF THE CERVIX ACCORDING TO GROSS CHARACTERISTICS OF THE TUMOR AND THE METHOD OF TREATMENT

TYPE OF TUMOR	IRRADIATION ONLY		PRIMARILY SURGICAL TREATMENT	
	CASES	PER CENT (OF 129)	CASES	PER CENT (OF 35)
Nodular	22	17.0	5	14.3
Papillary	54	41.9	14	40.0
Ulcerative	30	23.3	12	34.3
Polyp	1	0.8	1	2.9
Unknown	22	17.0	3	8.6

All the tumors were graded according to the method of Broders (Table VI). The average grade was 2.2. Of the patients presenting pain as a symptom the average grade of the lesion was 2.4 (Table VII).

TABLE VI. DISTRIBUTION OF 164 CASES OF ADENOCARCINOMA ACCORDING TO GRADE OF MALIGNANCY

GRADE	CASES	PER CENT (OF 164)
1	44	26.9
2	59	35.9
3	41	24.9
4	20	12.2

TABLE VII. DISTRIBUTION, ACCORDING TO GRADE OF MALIGNANCY, OF 59 CASES OF ADENOCARCINOMA OF THE CERVIX IN WHICH PAIN WAS THE PRESENTING SYMPTOM

GRADE	CASES	PER CENT (OF 59)
1	11	18.6
2	22	37.3
3	16	27.1
4	10	16.9

In 7 of the 35 patients treated primarily by surgical removal of the uterus, the carcinoma had extended beyond the cervix, and 3 of these patients underwent hysterectomy as a palliative procedure; it was recognized that not all the carcinoma tissue had been removed. In addition to surgical treatment, 23 patients had treatment also with radium or roentgen rays or both.

Among the 35 surgical patients, there was one hospital death, giving a hospital mortality of 2.9 per cent. One patient was untraced. Of the remaining 33 patients, 17 lived five years or more after operation, giving a five-year survival rate of 51.5 per cent.

Among the 129 patients who received radium therapy there was one hospital death, which gives a hospital mortality rate of 0.8 per cent. Five of these patients were untraced. Of the 123 remaining patients, 46 lived five or more years following treatment, giving a five-year survival rate of 37.4 per cent.

We believe that we found good correlation between the extent of anatomic involvement and the outcome of the disease, the gravity of the prognosis varying directly with the extent of anatomic involvement. No correlation was found relative to the degree of differentiation of the lesions and the outcome.

Nilsson,[2] who has reported a series of 80 cases of primary adenocarcinoma of the cervix, which is the largest reported series, classified cervical adenocarcinomas into six groups on the basis of the presenting histologic pattern. The necessity for the use of such a large number of groups emphasizes what others have demonstrated and also what we have found to be true of these neoplasms—that their histologic structure is extremely variable. No apparent constancy of histologic pattern is presented, even within groups of the same degree of differentiation. Many attempts were made by us to group patterns of a similar type, with the expectation of determining the comparative radiosensitivity of each pattern, but because of the great variability in structure and the marked overlapping of patterns, even from section to section taken from the same tumor, we were unable to be consistent in our attempts at such a classification (Figs. 1, *a* and *b*, 2, *a* and *b*, 3, *b* and 4).
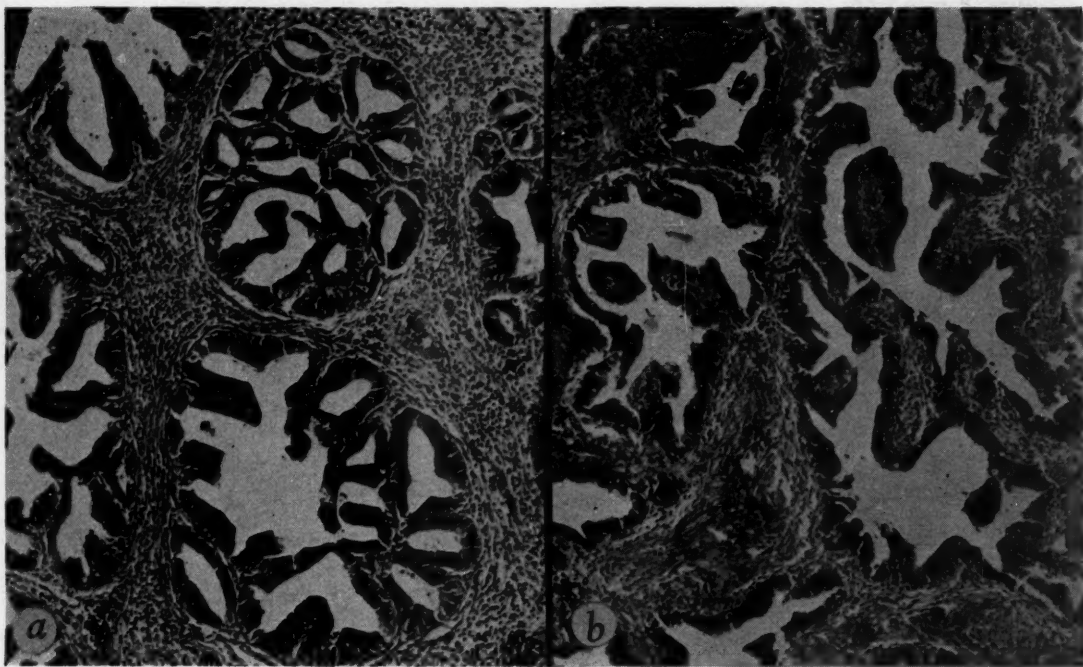
Fig. 1.—Adenocarcinoma of the cervix showing tendency toward mimicry of normal glandular structure. *a*, Grade 1. *b*, Grade 2. (Hematoxylin and eosin, ×100.)

Uncommonly encountered was a pattern consisting of ductlike structures lined with comparatively small, dark-staining, cuboidal or low columnar cells which were embedded in an abundant connective tissue base. This group of tumor types apparently represents the adenocarcinomas of the cervix which, Schiller[4] has postulated, have their origin from vestigial remnants of Gartner's duct. We were unable either to confirm or to deny this possibility (Fig. 2, *c*).

In only 9 instances (5.5 per cent) were we able to classify the neoplasm as a mucous (colloid) type of adenocarcinoma. The infrequency of occurrence of this type of neoplasm has been reported previously (Fig. 3, *a*).

It has been conclusively demonstrated in the past that most adenocarcinomas of the cervix have their origin in the glands or the ducts of the glands of the cervix. We have been able to demonstrate, on several occasions, the apparent origin of the neoplastic cells from the normal glandular elements (Fig. 2, *d*).

The average age of the 35 patients treated primarily by surgical means was 46.9 years while the average age of the 129 patients treated by irradiation was 51 years. This difference is, in all probability, explainable on the basis of the smallness of the number of cases in the surgical group plus the fact that all patients in this group had operative lesions and thus represented a more select group. The composite average age of 50.1 years closely approaches the average age of occurrence of squamous-cell carcinoma of the cervix.

The fact that only one patient in our series was less than 20 years of age is consistent with data given in published articles. Pollack and Taylor[3] in 1947
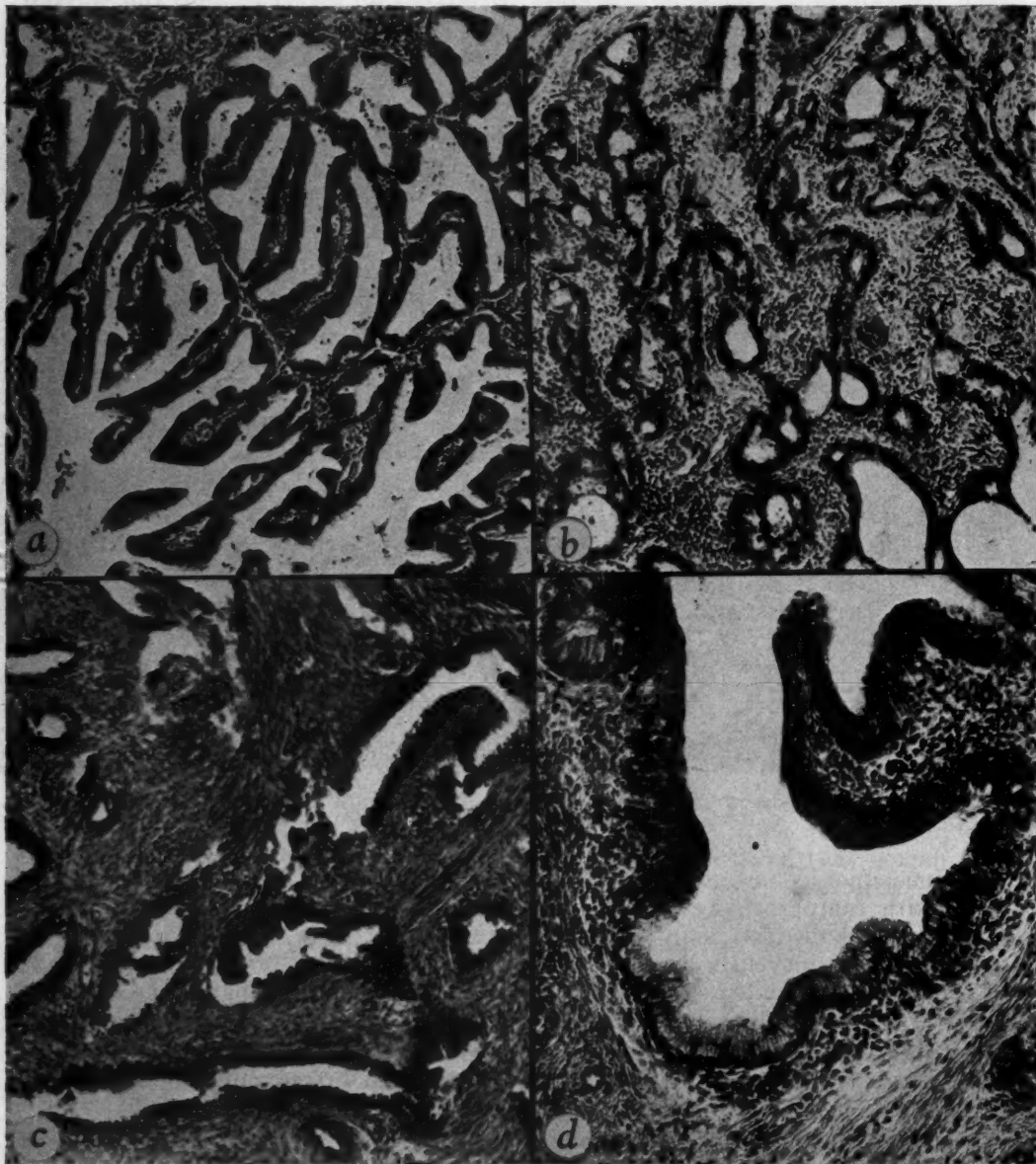
Fig. 2.—Grade 2 adenocarcinoma of the cervix stained with hematoxylin and eosin. a, Papillary structure. (×100.) b, Ductlike structures. (×100.) c, Ductlike structures lined with small dark-staining cuboidal cells, embedded in abundant connective tissue stroma. (×100.) d, Cervical gland lined partially with normal epithelium and partially with neoplastic cells which appear to be arising from the normal glandular elements. (×165.)

collected from the literature reports of 30 cases of cancer of the cervix occurring in patients during the first two decades of life. It is interesting to note, and it is possibly significant, that these authors found that 22 of their patients had adenocarcinoma, while only 4 had squamous-cell carcinoma; the lesions of the remaining 4 patients were unclassified. Only 4 of their 30 patients survived five years.

The presenting symptoms in our series of cases were similar to those reported by other authors. As would be expected, the symptoms are not unlike those presented by patients with the more common neoplasm of the cervix, squamous-cell carcinoma.
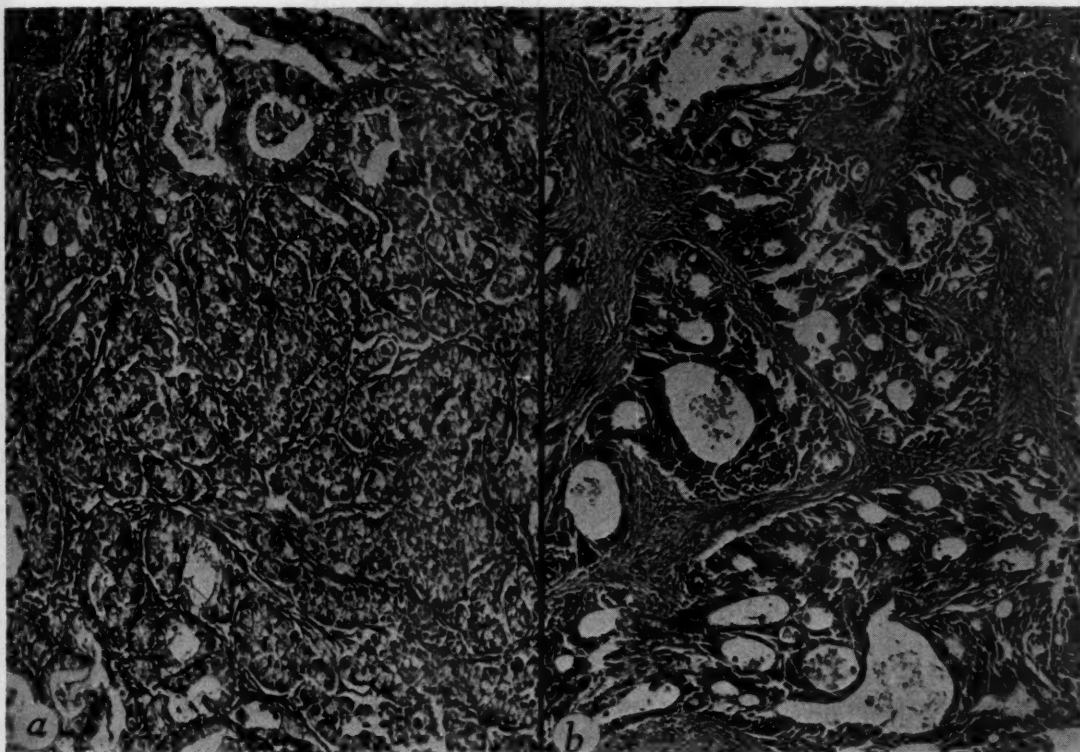
Fig. 3, *a* and *b*. Grade 3 adenocarcinoma of the cervix. (Hematoxylin and eosin. ×100.)

Pain is considered by many as indicating an advanced stage of the disease process. Our data would seem to substantiate this point of view—the average stage of anatomic involvement in our 153 cases in which the stage was known was 2.6, while in the 59 cases in which pain was the presenting symptom the average stage was 3.1.

No correlation was found between the duration of symptoms and the stage of anatomic involvement, the grade of the tumor, or the length of survival.

It is interesting to compare the distribution of our cases according to stage of anatomic involvement with a corresponding distribution of all cancers of the cervix as reported by Bowing and Fricke[1] in 1948 (Table VIII). It is obvious that 38.4 per cent of the adenocarcinomas which made up our series were in Stage 1 or 2, while in Bowing and Fricke's series only 15.6 per cent were in Stage 1 or 2 at the time of diagnosis.

When the outcome in the group in which the treatment was primarily surgical is compared with the outcome in the group in which treatment consisted of irradiation only, it seems, at first glance, that the treatment of choice consists of surgical measures plus irradiation. However, it must be recalled that certain factors favored the surgically treated group (Table IX). The age, stage of involvement by the tumor, grade of lesion, and percentage of patients with pain as a symptom were all lower in the group of patients treated surgically.
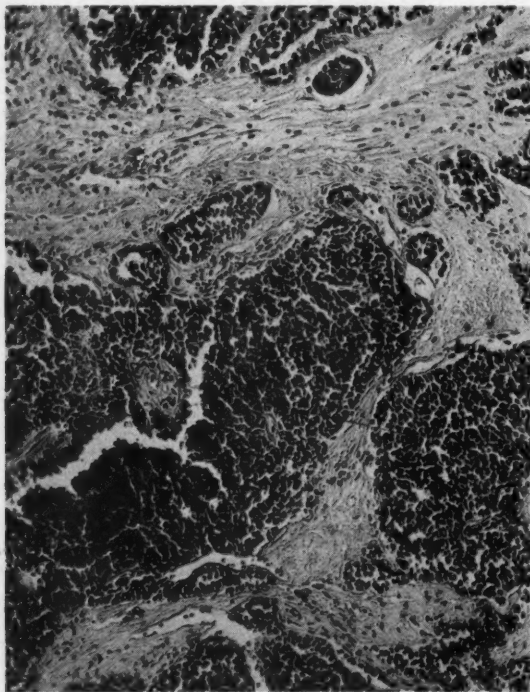
Fig. 4.—Grade 4 adenocarcinoma of the cervix (hematoxylin and eosin. ×100).

Thus it is apparent that no general treatment of choice can be set forth from these findings. It appears to us, however, that for patients who have adenocarcinoma of the cervix which can be classified clinically as operable and whose general condition will permit the risk of an extensive pelvic operation, an extensive surgical procedure is the treatment of choice. It appears logical that if the neoplasm in these selected cases has perchance already metastasized, and this must always be considered as a possibility, the surgical removal of the neoplastic nests in the regional lymph nodes is far surer of eradicating such foci of cancerous growth than is irradiation with roentgen rays or radium. We believe that our findings in part substantiate this line of reasoning.

Comparison of the five-year survival rate of 24.8 per cent found for patients with adenocarcinoma of the cervix treated by irradiation with roentgen rays or radium or both, with Bowing and Fricke's reported five-year survival rate of 32.8 per cent reported for all types of carcinoma of the cervix treated by irradiation, suggests that adenocarcinomas either are more radioresistant or are more prone to extend away from the primary growth by lymphatic channels than are squamous-cell carcinomas of the same region. This viewpoint is further substantiated by the fact that 38.4 per cent of the adenocarcinomas as compared with only 15.6 per cent of all carcinomas reported on by Bowing and Fricke were in Stage 1 or 2 at the time of diagnosis.

TABLE VIII. ADENOCARCINOMA OF THE CERVIX COMPARED WITH ALL CANCERS OF THE CERVIX FROM THE STANDPOINT OF STAGE OF ANATOMIC INVOLVEMENT

STAGE	ALL CANCERS OF CERVIX (BOWING AND FRICKE), PER CENT	ADENOCARCINOMA OF CERVIX (164 CASES), PER CENT
1	1.3	15.8
2	14.3	22.6
3	66.0	37.2
4	18.4	17.7
Unknown	—	6.7

TABLE IX. FACTORS FAVORING PRIMARILY SURGICAL TREATMENT OF ADENOCARCINOMA OF THE CERVIX OVER IRRADIATION ALONE

	SURGICAL TREATMENT (35 CASES)	IRRADIATION (129 CASES)
Average age, years	46.9	51.0
Average stage of lesion	2.1	2.7
Average grade of lesion	1.7	2.4
Pain, per cent of cases	22.9	39.4
Selection	Yes	No

Conclusions

On the basis of a review of the literature and a study of 164 cases of primary adenocarcinoma of the cervix, we conclude that:

1. This neoplasm represents approximately 4 to 5 per cent of all carcinomas of the cervix.

2. The average age of occurrence of this neoplasm is about 50 years, thus corresponding to the average age of occurrence of squamous-cell carcinoma of the cervix.

3. The occurrence of carcinoma of the cervix in patients less than 20 years of age is rare. One such case is included in our series. On the basis of Pollack and Taylor's collected series of such cases, one would conclude that the great majority of cervical carcinomas in young persons are adenocarcinomas.

4. As would be expected, the symptoms presented by patients with this tumor are not unlike those presented by patients with squamous-cell carcinoma of the same organ.

5. Pain as a symptom can usually be interpreted as indicating rather extensive involvement by the neoplastic process.

6. The stage of anatomic involvement is the best known prognostic index in regard to this type of cancer.

7. The gross appearance of adenocarcinoma presenting at the external os is not unlike that of squamous-cell carcinomas of the cervical labia.

8. The histologic structure is extremely variable, thus making impossible an absolute differentiation between primary endometrial and primary cervical adenocarcinoma by histologic examination alone.

9. Adenocarcinomas are apparently more radioresistant than are squamous-cell carcinomas of the cervix.

10. In selected cases, operative treatment with or without supplemental radiotherapy as indicated is the treatment of choice.

Addendum

Eighteen cases of mixed squamous-cell carcinoma and adenocarcinoma (adenoacanthoma) of the cervix were encountered incidentally during the study of adenocarcinomas arising primarily in the cervix (Fig. 5). These neoplasms were studied in the same manner as were the adenocarcinomas. Seventeen of these 18 cases were previously reported in detail by Skinner and McDonald,[5] to whose article the reader is referred for theories of histogenesis.
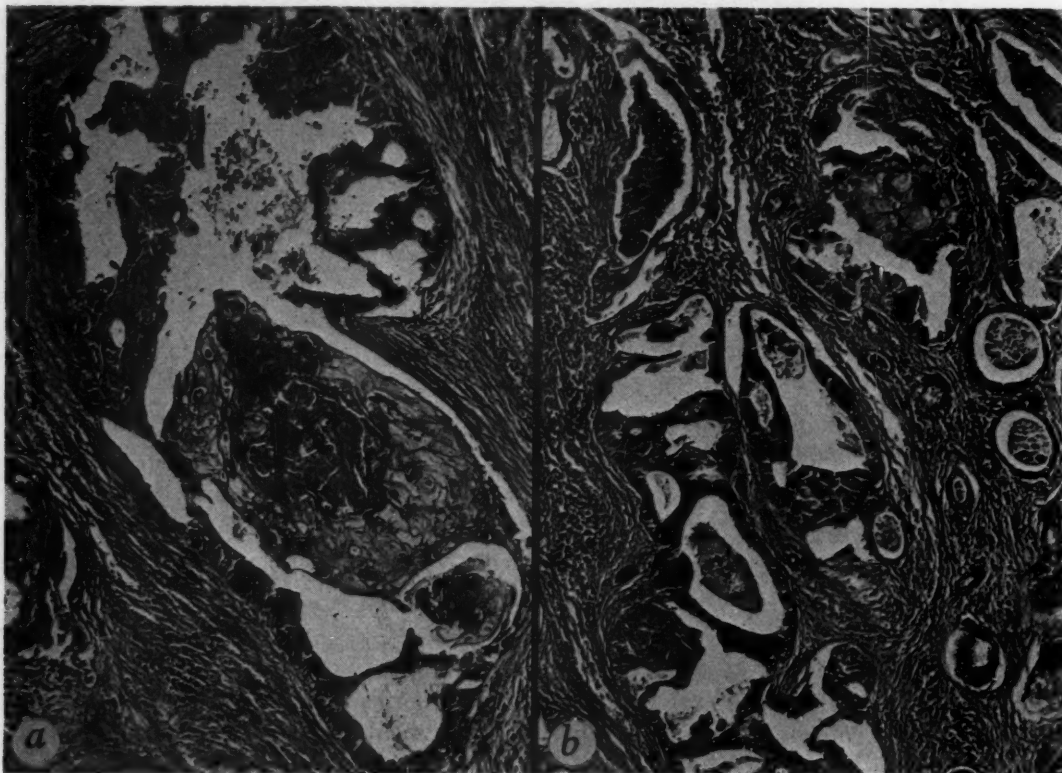

Fig. 5, *a* and *b*. Grade 2 mixed adenocarcinoma and squamous-cell carcinoma. The apparent origin of squamous cells is from the same base of cells as is the origin of neoplastic glandular cells. (Hematoxylin and eosin. ×100.)

It is felt that these tumors are different from primary adenocarcinomas of the cervix only in histologic appearance, and that the age of occurrence, the symptoms, the gross appearance of the tumors, the rate of growth as measured by the degree of malignancy, and the prognosis are not appreciably different from those of adenocarcinoma of the cervix as reported in our series.

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THE ETIOLOGY OF POSTPARTUM HEMORRHAGE

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(From the Ellis Hospital)

POSTPARTUM hemorrhage is defined as bleeding in excess of 500 ml. within the first twenty-four hours after birth, including third stage bleeding and bleeding from episiotomy.[1]

As a cause of maternal death, postpartum hemorrhage ranks high,[2] and is estimated by McGee as causing 30 per cent of maternal deaths.[3] This type of bleeding kills directly by producing shock, and kills indirectly by lowering resistance to infection. It is fitting that we should study and prevent this complication where possible.

Material

Accordingly, a review has been made of the recognized cases of postpartum hemorrhage occurring at the Ellis Hospital in the four-year period 1947 to 1950, inclusive.

Ellis Hospital is a 400-bed general hospital with a well-regulated obstetrical service, privileges being granted to physicians in proportion to training, ability, and experience. There is one obstetrical resident. There are nine specialists with full privileges, of whom five are Diplomates of the American Board of Obstetrics and Gynecology. Sixty-one general practitioners are privileged to manage normal labor, perform outlet forceps and episiotomy, and repair first- and second-degree lacerations. Eight physicians have intermediate privileges. Mismanaged cases are brought into open discussion at a monthly meeting.

Blood loss at delivery is measured with the aid of a blood basin included under a rubber drape. The occurrence of postpartum hemorrhage in other instances has necessarily been judged by estimation by the attending physician, the house staff, and the obstetrical nurses, nevtreheless undoubtedly giving rise to considerable error.

During the period studied there were 7,326 deliveries, including 416 cesarean sections (5.7 per cent). Seven thousand four hundred sixteen babies were delivered, including 86 sets of twins and two sets of triplets. Among the 6,910 vaginal deliveries, 190 postpartum hemorrhages were recognized, an incidence of 2.7 per cent. No instance of postpartum hemorrhage was noted among the cases of cesarean section, although blood loss at operation in many of these undoubtedly exceeded 500 ml.

Four maternal deaths occurred in this period, one of which was due to postpartum hemorrhage. The maternal death rate at Ellis Hospital during the period studied was therefore 5 per 10,000 deliveries, while the maternal mortality rate in the United States in 1946 was 16 per 10,000 live births.*

An attempt was made at first to determine the cause of each hemorrhage from the hospital record. The results by this method were unsatisfactory because the cause could be fairly definitely determined or surmised in only 83 cases. These are listed in Table I.

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*Data from the National Office of Vital Statistics, Federal Security Agency, United States Children's Bureau.

"Difficult operative delivery" signifies any delivery in which the extensiveness of the procedure used (such as midforceps), combined with the duration of anesthesia and the time required to repair episiotomy and lacerations, was the apparent cause of blood loss exceeding the normal limit. Blood loss in these cases varied from 525 to 1,500 ml.

TABLE I. THE CAUSE OF POSTPARTUM HEMORRHAGE AS DETERMINED FROM THE HOSPITAL RECORD

Difficult operative delivery	43
Bleeding from lacerations and/or episiotomy	12
Third stage bleeding	19
Laceration of cervix	5
Retained placental cotyledon	1
Low implantation of placenta	1
Traumatic rupture of lower uterine segment	1
Repair of rectocele	1

"Third stage bleeding" indicates that excessive blood loss was associated with delayed delivery of the placenta, the potential retroplacental hematoma escaping past a separated margin of the placenta, or that the placenta was retained in the upper uterine segment and required manual extraction with its attendant dangers of atony of the uterus following deep ether anesthesia, and laceration of the uterine wall.[4] Greenhill[5] emphasizes, however, that threatened postpartum hemorrhage due to third stage bleeding should be prevented by manual extraction of the placenta.

"Retained placental tissue" is a rare cause of postpartum hemorrhage, but ranks high as a cause of puerperal bleeding.[6]

The oxytocic routine at this hospital should be mentioned. In most instances, 1 ml. of Pitocin (10 units) is administered intramuscularly immediately after the birth of the baby. After delivery of the placenta, 0.2 mg. of ergonovine is given intramuscularly. This routine is varied by some, 0.25 ml. of Pitocin being given intravenously with the birth, and the remainder of the Pitocin and the ergonovine being given intramuscularly with the placental exit. One obstetrician gives the ergonovine intravenously at delivery of the baby's anterior shoulder. Another uses methylergonovine by the latter technique.

As demonstrated by others as well as by a study in this hospital,[7] intelligent use of the oxytocics can reduce blood loss to a minimum. The most important detail in the over-all diminution of blood loss, however, would seem to be a vigilant observation of the activity of the fundus, especially under general anesthesia, whereby gross relaxation of the fundus quickly following the third stage and occasioning undue loss of blood can be prevented.

Five patients in this series were recognized as harboring primary blood dyscrasias, but not one of these incurred abnormal blood loss within the twenty-four hours following delivery. There were two patients with thrombocytopenic purpura, one patient with macrocytic anemia of pregnancy, one with nocturnal paroxysmal hemoglobinuria, and one with Hodgkin's disease. The course of a known hemophilia carrier was uneventful. A frequent occurrence of physiological anemia of pregnancy and hypochromic iron-deficiency anemia was noted without abnormal bleeding tendency.

It is apparent that a consideration of the cause of postpartum hemorrhage in the individual instances has not given a satisfactory explanation for most of the cases. It was therefore believed that a more illuminating study would be a statistical analysis of any significant factors in all the cases, and that in this way some more satisfactory conclusions might be reached. The factors will be presented in Tables II to VI and Figs. 1 to 5.

TABLE II. PARITY, AND NUMBER AND SIZE OF BABIES AS RELATED TO THE INCIDENCE OF
POSTPARTUM HEMORRHAGE

CONDITION	NUMBER OF TIMES CONDITION PRESENT	INCIDENCE OF POST-PARTUM HEMORRHAGE
Primigravidity	3,038	3.6%
Multiparity	4,288	1.8%
Fifth or later pregnancy	276	0.7%
Multiple pregnancy	88	3.3%
Premature delivery	530	1.3%
Baby weighing 9 pounds or more	234	6.9%
Expected incidence of postpartum hemorrhage in this series, among vaginal deliveries		2.7%

It is clear that postpartum hemorrhage is twice as likely to occur in a primigravid parturient as in a multipara.

Grand multiparity (fifth or later pregnancy) appears to be particularly benign as far as risk of excessive bleeding is concerned. This observation is not in agreement with the general consensus that this group runs a greater risk of hemorrhage than other parity groups.

Multiple pregnancy is recognized as a predisposing cause of postpartum bleeding, but this predisposition, apparently the result of overdistention of the uterus with subsequent atony, is even more marked in the group wherein the baby weighed 9 pounds or more. The tendency to greater cervical, vaginal, and perineal injury is obvious in the latter condition.

Premature delivery is less likely to be associated with excessive blood loss than term delivery.

TABLE III. MODE OF VAGINAL DELIVERY AS RELATED TO THE INCIDENCE OF
POSTPARTUM HEMORRHAGE

MODE OF DELIVERY	OCCURRENCE OF THIS MODE OF DELIVERY	INCIDENCE OF POST-PARTUM HEMORRHAGE
Spontaneous cephalic	4,546 cases	1.1%
Breech delivery (assisted or extracted)	298 cases	2.0%
Low forceps	1,791 cases	4.9%
Midforceps	253 cases	14.2%
Internal podalic version	22 cases	50 %

It is very clear that the more extensive the operative procedure necessary for delivery, the more likely is postpartum hemorrhage.

TABLE IV. TYPE OF ANESTHESIA AS RELATED TO THE INCIDENCE OF POSTPARTUM
HEMORRHAGE

TYPE OF ANESTHESIA	NUMBER OF SUCH ANESTHETICS ADMINISTERED FOR VAGINAL DELIVERY	INCIDENCE OF POST-PARTUM HEMORRHAGE
Nitrous oxide, oxygen, and ether	5,341	2.9%
Open drop ether	717	3.1%
Nitrous oxide and oxygen	524	1.1%
Spinal	141	4.3%
No anesthesia	98	2.0%
Caudal	46	0.0%
Local and/or pudendal block	42	0.0%
Cyclopropane	2	0.0%

It is apparent that, over a large series of cases, ether used in the anesthesia for delivery is associated with a higher incidence of postpartum hemorrhage than any other anesthetic.

Analysis of the only six cases of hemorrhage occurring with the use of nitrous oxide and oxygen revealed that one was associated with pre-eclampsia and premature separation of the placenta, one with pre-eclampsia and primary inertia, two with difficult operative deliveries, and one with manual extraction of the placenta subsequently under ether anesthesia. Nitrous oxide without ether definitely does not predispose to postpartum hemorrhage.
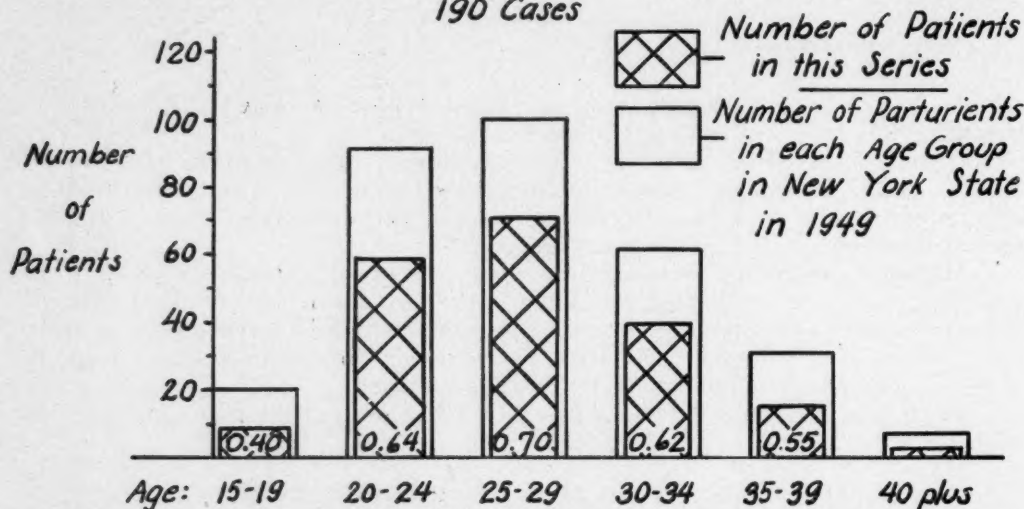
Fig. 1.—The decimal figure at the base of each column represents the ratio between the number of patients in each particular age group in this series, and the number of women in this same age group who delivered babies in New York State in 1949. From these figures, it is evident that the parturient age group in which postpartum hemorrhage is most likely is the 25- to 29-year or middle group, with diminution toward either extreme. This dispels a commonly held notion that the older age group is most likely to hemorrhage.

Figures by courtesy of the Office of Vital Statistics of the New York State Department of Health. The figure 100 at the left in Fig. 1 indicates 100,000 patients in the State figures.
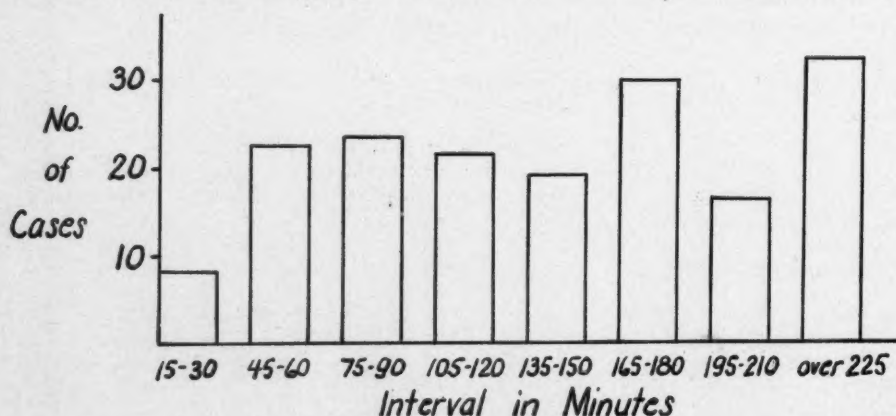

Fig. 2.—The dose of meperidine used was 100 mg. intramuscularly as a rule. The distribution of times of administration of the drug appears to be that which might be expected in any series. We know that the most common cause of primary uterine inertia in modern obstetrics is the injudicious use of analgesics,[3] but there is no convincing evidence on this graph that analgesia is related to excessive bleeding.

*Demerol (Winthrop-Stearns, Inc.).

The figure given for hemorrhage under spinal anesthesia is misleading because many of these cases comprised a pilot series in the use of spinal anesthesia in obstetrics in this hospital,[9] during which the anesthetic was frequently administered too early, thus necessitating extensive operative procedures which have been shown above to be associated with bleeding. Here, again, analysis of the six cases of postpartum hemorrhage occurring with spinal anesthesia revealed that four were associated with other difficulties, namely, two difficult operative deliveries, one second-degree laceration of the perineum with excessive bleeding, and one pre-eclampsia in an isoimmunized Rh-negative woman. Spinal anesthesia does not apparently lead to hemorrhage other than by relaxing the perineal blood vessels.
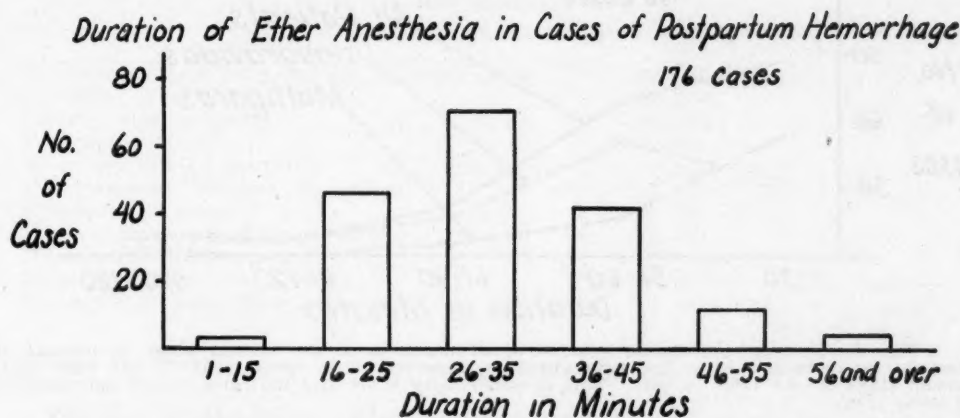

Fig. 3.—It is noted that a majority of the patients in this group inhaled ether for more than twenty-five minutes. The obstetrician must keep a clock in his head to eliminate this added factor of prolongation of anesthesia. The onset of anesthesia in each case was judged to be the time at which the patient was made unconscious.

The incidence for delivery without anesthesia is again misleading, because one of the two hemorrhages in this group was associated with manual extraction of the placenta subsequently under ether anesthesia, and the other with precipitate delivery of a stillborn macerated fetus in an Rh-negative, isoimmunized patient.

The figures for caudal, local, and cyclopropane anesthesia are very gratifying, but rather small in numbers for significance.

Grouping of the hemorrhage cases according to the amount of blood loss showed that ether anesthesia was consistently associated through all the groups, both under and over 1,000 ml. On the other hand, no patient receiving spinal anesthesia lost more than 1,000 ml. of blood.

Table V demonstrates a nice correlation between the incidence of postpartum hemorrhage and the extent of outlet surgery, the more extensive procedures being associated with a higher incidence.

TABLE V. OUTLET SURGERY AS RELATED TO THE INCIDENCE OF POSTPARTUM HEMORRHAGE

PROCEDURE	NUMBER PERFORMED	INCIDENCE OF HEMORRHAGE
Episiotomy and repair	4,320	3.7%
Repair of first degree lacerations	853	2.9%
Repair of second degree lacerations	166	12.6%
Repair of third degree lacerations	14	7.1%
Repair of cervical lacerations	49	49.0%
Repair of rectocele	1	100 %

Manual extraction of the placenta has been associated with postpartum hemorrhage in 33 per cent of instances in this series. This is a significant figure, emphasizing the gravity of the procedure.

The association of postpartum hemorrhage with prolonged labor and primary uterine inertia appears to be parallel in the two conditions, which are often coexistent. The general incidence of prolonged labor in this series would be about 2 per cent,[10] whereby the nineteen hemorrhages in this group signify a 15 per cent occurrence of bleeding following prolonged labor.. This is a significant factor.
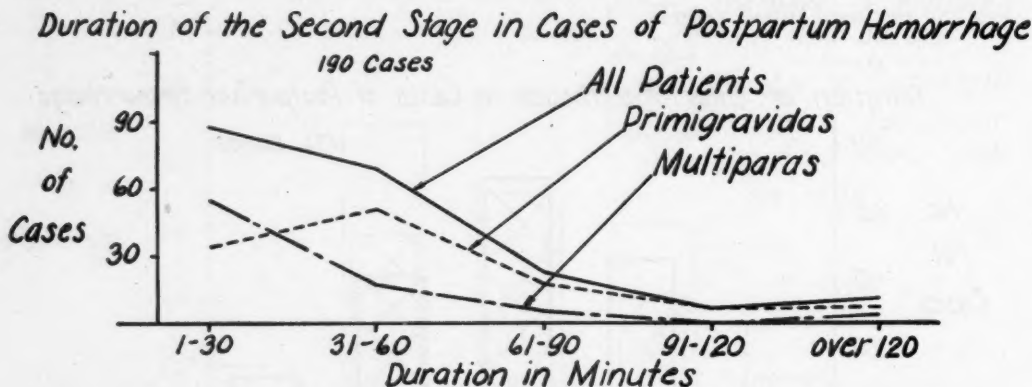

Fig. 4.—For the multiparas, the curve of duration of the second stage is normal and requires no comment. For the primigravidas, however, it is noted that 75 per cent had a second stage of one hour or less. This is abnormally short and indicates forced accouchement of some type.
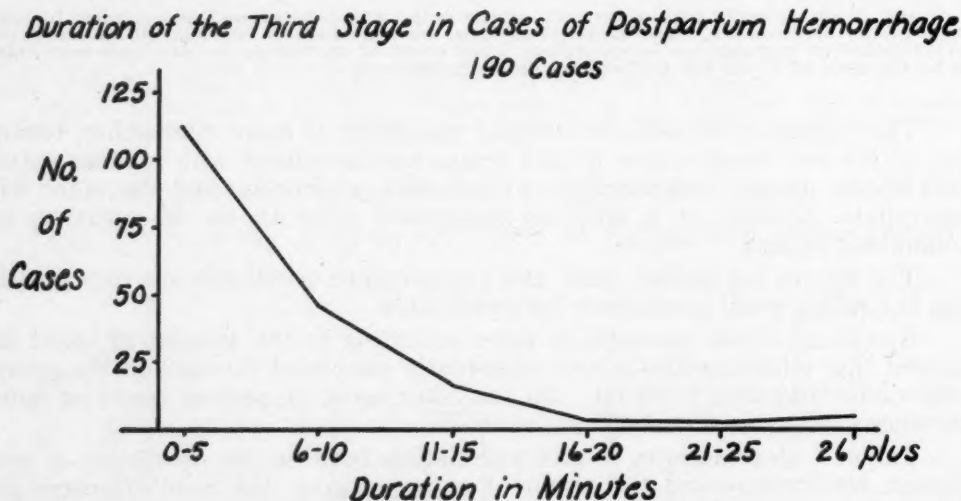

Fig. 5.—The cases with long third stages are generally those in which manual extraction of the placenta was performed. The curve otherwise appears normal.

Precipitate labor and secondary uterine inertia do not lead to postpartum hemorrhage of themselves.

Postpartum bleeding with eclampsia and pre-eclampsia is similar in incidence, and significantly high (16 to 17 per cent). It is well known that ante- and intrapartum bleeding also occur very frequently in these conditions.

Hypertension without other toxemia is uncommon, therefore the three hemorrhages in this group might be considered definitely related to the hypertension.

Hydramnios was not a factor in the causation of bleeding in this series.

Rh-negativity per se definitely does not predispose to postpartum hemorrhage, the incidence in this series being very close to the expected.[11] However, the incidence among isoimmunized Rh-negative women is greatly out of proportion to the expected. About 5 per cent of Rh-negative women become sensitized following pregnancy or transfusion.[12] Sixteen per cent of the Rh-negative women having postpartum hemorrhage in this series were sensitized, more than three times the expected incidence. When stillbirth is associated with isoimmunization, Weiner[13] has demonstrated fibrinogenopenia with a deficient clotting mechanism in the mother.

TABLE VI. CERTAIN COMPLICATIONS AS RELATED TO THE INCIDENCE OF POSTPARTUM HEMORRHAGE

COMPLICATION	HEMORRHAGE ASSOCIATED
Retained placenta, extracted manually (67 cases)	22 cases (33%)
Prolonged labor	19 cases
Primary uterine inertia	16 cases
Precipitate labor	2 cases
Secondary uterine inertia	2 cases
Pre-eclampsia (168 cases recognized)	27 cases (16%)
Eclampsia (6 cases)	1 case (17%)
Hypertension without other toxemia	3 cases
Hydramnios (16 recognized)	0 cases
Rh-negativity	25 cases (13.3% of series)
Rh-negativity with isoimmunization	4 cases (16% of Rh-negative women with hemorrhage)

The Sex of the Baby.—The possibility that the sex of the baby might be a factor in the causation of bleeding, with some hormonal change affecting the placental site, was considered. Tallying revealed an almost exact similarity in incidence with each sex. This is a gratifying reflection on the reliability of the figures presented.

Summary

A survey is made of 190 recognized postpartum hemorrhages which occurred among 6,910 vaginal deliveries over a four-year period in a 400-bed general hospital, an incidence of 2.7 per cent.

There was one maternal death from postpartum hemorrhage during this period.

A multiplicity of factors determines blood loss in any vaginal delivery, and the optimal method of prevention would be to know the cause in each particular instance. Analysis of the individual hospital records divulged the cause of postpartum hemorrhage in only 83 of 190 cases. The next best method of approach for determining the cause was deemed to be the statistical; therefore, the records were analyzed from this standpoint.

Conclusions

There is no single cause of postpartum hemorrhage.

The causes of, and factors predisposing to, postpartum hemorrhage might be listed approximately as follows, in order of importance:

1. Third stage bleeding, including manual extraction of the placenta
2. Difficult operative delivery
3. Eclampsia and pre-eclampsia
4. An overly large baby (about 9 pounds or more)

5. Ether anesthesia, especially if prolonged

6. A short second stage of labor in a primigravida, i.e., accouchement forcé

7. Cervical, vaginal, and perineal lacerations

8. Multiple pregnancy

9. Isoimmuunization of an Rh-negative woman

10. Episiotomy

11. Primigravidity

12. The patient in the mild-childbearing period

13. Prolonged labor and primary uterine inertia

14. Hypertensive toxemia of pregnancy

15. Retained secundines

16. Low implantation of the placenta

17. Factors as yet unknown

Procedures and factors which did not predispose to postpartum hemorrhage in this series were as follows:

1. Certain types of anesthesia: nitrous oxide-oxygen; and probably local, regional, and no anesthesia

2. Precipitate labor

3. Secondary uterine inertia

4. The sex of the baby

5. Multiparity, including grand multiparity

6. Premature delivery

7. Spontaneous cephalic delivery

8. Hydramnios

9. Rh-negativity per se

10. The oxytocic treatment, provided the medication is adequate

11. Primary blood dyscrasias. These were conspicuously absent in the causation of postpartum hemorrhage in this series

12. The patient aged over 35 years

13. General analgesia

No statement can be made regarding the influence of primary breech delivery, because premature breech deliveries, assisted breech deliveries, and breech extractions have been grouped together in this series.

Consideration of the factors leading to postpartum hemorrhage will help us to manage pregnancy, labor, delivery, and the postpartum period in such a way as to reduce to a minimum this very serious complication.

The Record Room staff under Miss Louise S. Haughton, and Miss Janice C. Cronin, R.N., of the Delivery Room, rendered invaluable assistance in the preparation of charts and statistics.

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10 B 2 SHERIDAN VILLAGE

MORBIDITY AFTER CESAREAN SECTION*

A Clinical Evaluation of Prophylaxis With Aureomycin in 100 Consecutive Cases

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PRIOR to the last decade infection was a frequent cause of death following cesarean section. Percentage of mortality caused by sepsis was recorded as follows: 48 per cent of a 2.96 per cent mortality from 1923 to 1938 in the Woman's Hospital of the State of New York[1]; 49 per cent of a 5.9 per cent mortality from 1927 to 1936 in the hospitals of New Orleans[2]; 46.15 per cent of a 6.8 per cent mortality in 1931 in the hospitals of Philadelphia[3]; 35 per cent of an 0.8 per cent mortality from 1931 to 1938 in the Chicago Lying-in Hospital[4]; 36.36 per cent of a 2.46 per cent mortality in 1941 in the hospitals of Philadelphia.[3]

During the last few years postsection deaths due to infection have become rare in obstetric centers. More than 1,000 consecutive cases without such deaths have been reported by D'Esopo,[5] Dieckmann,[6] Verch,[7] Lull,[8] and McLean.[9] In New Orleans, mortality due to infection after section has become rare in private institutions. Since 1944 over 1,100 consecutive cesarean operations have been done at the Southern Baptist Hospital without mortality. At Charity Hospital the rates for 1943, 1947, and 1950 were, respectively, 0 per cent of 1.02 per cent mortality, 0 per cent of 1.41 per cent mortality, and 0 per cent of 1.08 per cent mortality.

This degree of improvement should not lead to complacency, because deaths from sepsis are preventable and the possibility of such deaths occurring is frequently encountered. Moreover, obstetricians are not concerned with saving lives alone, but have the responsibility of the control of illness. When morbidity following cesarean operations is considered, the degree of improvement is not so marked. Table I lists some morbidity figures.[2, 6, 7, 9, 10, 11, 12]

Before attempting analyses of groups of cases it is well to consider some of the variables encountered. At the outset one realizes that there is no single absolutely reliable clinical indicator of presence or degree of infection. The most commonly used indicator is fever. Morbid temperatures may be caused by dehydration, reaction to foreign substances (infusions, blood, drugs), intraperitoneal spillage of blood and/or amniotic fluid, damage to heat regulation (shock, anoxia, hemorrhage), atelectasis, or by infection not related to

cesarean section. Objective evidence at the sites of infection may exceed or be less than the degree of fever. At times localized signs are absent to ordinary means of examination even though infection is present. In spite of these facts being true, fever appears to be the best single indicator and is relatively reliable when correlated with other findings.

TABLE I. CESAREAN SECTION, MORBIDITY

YEARS	HOSPITALS	PER CENT MORBID
1931-49	Chicago Lying-in	47 to 20
1921-26	City of New Orleans	63.5
1927-36	City of New Orleans	61.3
1920-38	Methodist Hospital, Brooklyn	50
1935-46	Norfolk, Va. (Private cases)	13.1-14.6
1943	Cincinnati General	67
1945-47	Millard Fillmore (Buffalo)	25.2
1943-47	Milwaukee	15.2
1949	Cincinnati General	30
1950	Southern Baptist Hospital, New Orleans	8
1937	Charity Hospital of New Orleans	66
1943	Charity Hospital of New Orleans	62
1947	Charity Hospital of New Orleans	50

Not only are the recognition and recording of infection a relative matter, but cause of infection involves many factors. The sources of bacteria may be endogenous or exogenous. Of the endogenous, in modern obstetrics those present in the vagina assume first order of importance. Their infectivity is related to species, virulence, and concentration. It is suggested that personal hygiene has much to do with this, since higher degrees of infectivity are more common among mothers of the less fortunate economic, intellectual, educational, and social levels. Spread from adjacent areas, mouth, or lesions at times occurs. Exogenous sources include obstetricians, nurses, other patients, spectators, and equipment.

When pathogenic bacteria are present in the vagina, as they usually are to some degree, spread may occur by labor, examinations, or operations (stripping of membranes, rupture of membranes, conversion, version, attempt at forceps delivery). These means of spread have been duly incriminated in numerous publications and of them we are fully aware. Their individual degree of importance in any given case is related to other factors favoring infection and to the employment of prophylactic and definitive therapy, so that in a group of cases absolute statistical analysis is not reliable in that the other factors involved do not remain constant. Hence varying opinions are expressed in regard to the importance of duration of labor, rupture of membranes, and type of examinations.

Of considerable importance is the response of the mother to contamination. Anemia, inadequate nutrition, diabetes, toxemia, trauma, fatigue, and systemic disease may appreciably decrease resistance to infection.

Operative technique may involve other variables. These include the type of section—classical, lower segment, extraperitoneal, or section hysterectomy. It would appear that the operation per se does not cause infection when prop-

erly performed, but the degree of contamination of the peritoneal cavity, hemostasis, and trauma to tissues have their influence. Complications of anesthesia may lead to extraabdominal infection.

Preventive therapy involves many variables. Vaginal instillations are not presently as commonly used in this locality as they were formerly. Prophylactic parenteral or oral administration of antibacterial agents is being more frequently used. Local application into wounds has been practically discontinued. Total obstetric care is improving due to more trained obstetricians, better educated patients, and better hospital facilities so that situations favorable to infection are less common.

MAXIMUM DAILY TEMPERATURES
100 CONSECUTIVE CESAREAN SECTIONS
AT
SOUTHERN BAPTIST HOSPITAL
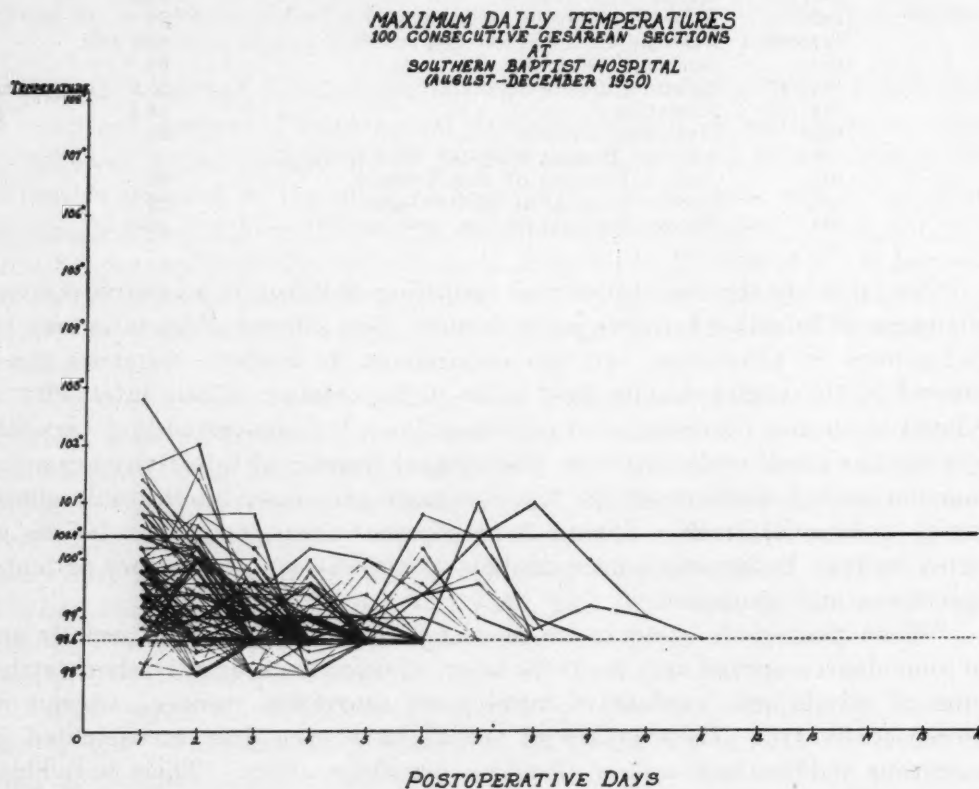(AUGUST–DECEMBER 1950)

POSTOPERATIVE DAYS

Fig. 1.

Consideration of definitive therapy involves variation as to (1) the use of operations to avoid or limit spread of infection, (2) the use of effective and less toxic antibacterial agents, and (3) the employment of better preoperative and postoperative care as concerns use of blood, fluids, electrolytes, oxygen, intestinal decompression, ambulation, etc. Certainly these factors influence the control of infection. They are all of importance and to imply that employment of one particular operation or use of certain antibacterials obviates adequate employment of other means of therapeusis is illogical. Choice of operation is to be decided for each patient and is partially dependent on factors other than those concerning infection (such as future childbearing or indica-

tions for hysterectomy). That antibacterial administration allows the retention of infected uteri and decreases the necessity for extraperitoneal approach to uterine section has been indicated by local experience and reports of Douglas,[13] Dantuono,[14] and Kobak.[15] That extraperitoneal section limits to some extent the spread of infectious material is evident. That hysterectomy limits spread of infection has been recognized. Decision as to the type of operation to be employed is properly determined by evaluation of extent of advantages and disadvantages in each case.

Material

The principal purpose of this discussion is to attempt to evaluate the effectiveness of aureomycin administered prophylactically. Many patients do not need preventive antibacterial therapy. This is indicated by the infrequency of morbid temperature curves noted in the records of 100 consecutively

MAXIMUM DAILY TEMPERATURES
100 CONSECUTIVE CESAREAN SECTIONS
AT
CHARITY HOSPITAL OF NEW ORLEANS
TULANE OBSTETRICAL SERVICE
AUGUST 1949 – MARCH 1950
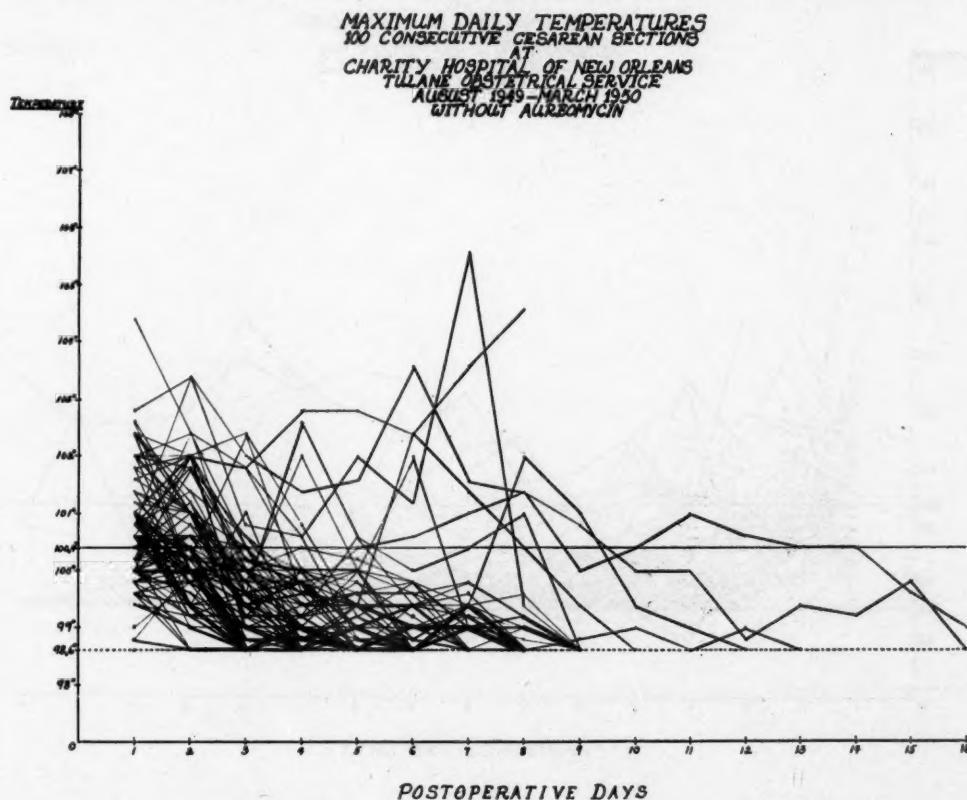WITHOUT AUREOMYCIN

POSTOPERATIVE DAYS

Fig. 2.

sectioned mothers at Southern Baptist Hospital from Aug. 1, 1950, to December, 1950 (Fig. 1). These results are associated with patients of average or better economic and educational status, for the most part under the care of well-trained obstetricians. Less than one-half of them received any antibacterial agent. Sixty-six of these mothers were sectioned without labor, ruptured membranes, bleeding, toxemia, or serious systemic disease, with a morbidity rate of 5.3 per cent. Of a total of 10 mothers with labors of over 12 hours and more than 3 examinations, 6 of whom had membranes ruptured over

12 hours (7 of whom had prophylactic penicillin) only 2 exhibited febrile temperature curves. Of the 8 morbid cases, 4 were elective sections (2 "repeats," 2 "disproportions," 1 had 48 hours' labor with inertia, 1 had 8 hours' labor with disproportion, 1 had 14 hours' labor with disproportion, and 1 had placenta previa).

To be contrasted with this group are 100 consecutive patients operated upon on the Tulane School of Medicine Obstetric Service at Charity Hospital from Aug. 1, 1949, to March 3, 1950 (Fig. 2). The mortality due to infection was 0 per cent of a total of 2 per cent. The morbidity rate was 40 per cent. Perusal of the duration and maximum degree of fever indicates that extent of illness was even higher than percentage variation in morbidity indicates when compared with the Baptist Hospital series. Ninety-seven per cent of these patients received some antibacterial. None received aureomycin; however, penicillin, sulfadiazine, and streptomycin were available for use as indicated.

MAXIMUM DAILY TEMPERATURES
50 UNSELECTED CESAREAN SECTIONS
AT
CHARITY HOSPITAL OF NEW ORLEANS
L.S.U. OBSTETRICAL SERVICE
DECEMBER 1948 — SEPTEMBER 1949
NO PROPHYLACTIC ANTIBACTERIALS
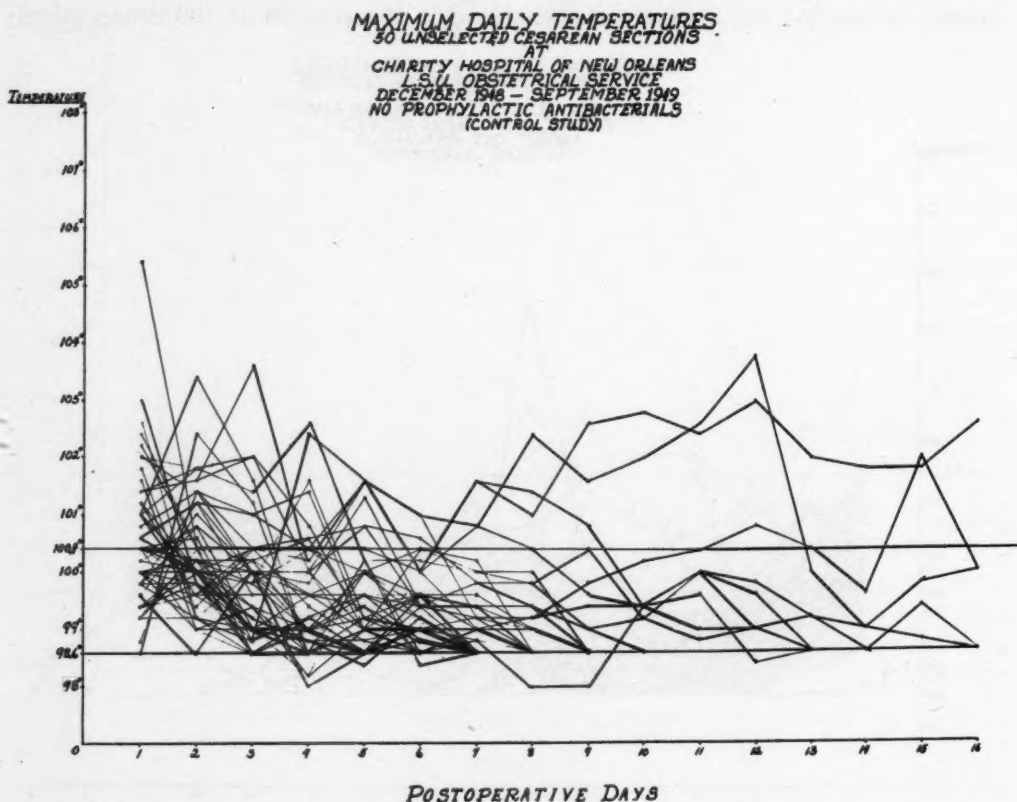(CONTROL STUDY)

POSTOPERATIVE DAYS

Fig. 3.

Only 19 of these patients were sectioned without labor, ruptured membranes, bleeding, toxemia, serious systemic disease, or more than one examination. Of the 19, 31 per cent were morbid. Of the 12 patients with labors of over 12 hours and more than 3 examinations, 5 (41.7 per cent) had morbid temperatures.

Through the courtesy of the Louisiana State University School of Medicine, Department of Obstetrics, maximum daily temperatures of 50 patients without prophylactic antibacterials (control study) operated upon from December, 1948, to September, 1949, at Charity Hospital of Louisiana at New Orleans are recorded (Fig. 3). The morbidity was 30 per cent without a death.

Of 15 patients without labor, ruptured membranes, more than one examination, bleeding, toxemia, or serious systemic disease, only 2 were morbid (13.3 per cent). Of 12 with labor of over 12 hours and over 3 examinations, 6 were morbid. Therapy was given as indicated in the postoperative period, but it is notable that duration of fevers was longer than in the two previous series mentioned.

Guilbeau and associates[16] reported bacteriological and clinical investigation of aureomycin in obstetrics. It appeared that this antibiotic had a greater range of effectiveness than any single drug evaluated in obstetrics. Consequently, begining Aug. 1, 1950, prophylactic administration of aureomycin was instituted for all section cases on the Tulane Obstetrical Service at Charity Hospital. Each patient received three 500 mg. intravenous doses of aureomycin in infusions (at the time of operation, 12 hours and 24 hours postoperatively). A similar dose was given to section candidates during labor. No

MAXIMUM DAILY TEMPERATURES
100 CONSECUTIVE CESAREAN SECTIONS
AT
CHARITY HOSPITAL OF NEW ORLEANS
TULANE OBSTETRICAL SERVICE
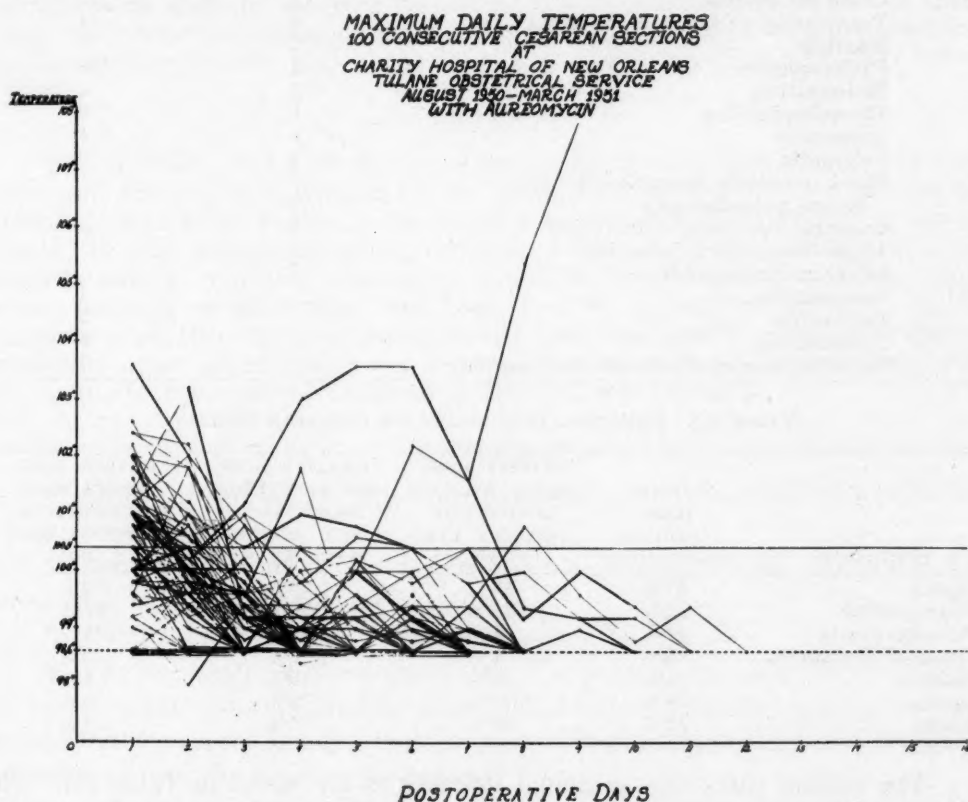AUGUST 1950—MARCH 1951
WITH AUREOMYCIN

POSTOPERATIVE DAYS

Fig. 4.

other prophylactic agent was used but 35 received penicillin and/or streptomycin and/or sulfonamides during their postoperative stay. The temperature graph (Fig. 4) of these cases reveals considerable change as compared with 100 cases on this same service one year before. The morbidity was 30 per cent and it is evident that duration of fevers was shorter. However, this group of cases includes 41 patients without labor, ruptured membranes, more than 1 examination, bleeding, toxemia or serious systemic disease, as contrasted with 19 in the series of 100 without aureomycin. Of these patients 17 per cent were mildly morbid. Of 14 mothers sectioned after labors of over 12

hours with more than 3 examinations, 3 were morbid. In none of the 3 cases did the morbid temperature continue over 3 days.

The pathologic states associated with fevers are noted in Table II. The instances listed as "cause not evident" are comprised principally of patients with 2-day fevers, which may have been due to intraperitoneal blood, ileus, or mild endometritis. Unfortunately pyrogenic reactions caused by infusions and transfusions were common and serve to confuse the picture. It would appear that aureomycin had reduced the incidence of urinary-tract infection, clinically evident parametritis, and pelvic peritonitis.

TABLE II. CAUSES OF POSTSECTION MORBID TEMPERATURES, TULANE OBSTETRICAL SERVICE OF CHARITY HOSPITAL

	AUREOMYCIN SERIES	WITHOUT AUREOMYCIN
Cause not evident	12	20
Transfusion or infusion reactions	6	4
Mastitis	2	1
Pyelonephritis	2	15
Endometritis	1	2
Thrombophlebitis	1	0
Atelectasis	1	1
Eclampsia	1	0
Shock, complete abruptio placentae, severe pre-eclampsia	1	
Incompatible blood transfusion	1	
Upper respiratory infection	1	
Lower nephron syndrome	1	
Pneumonitis		1
Peritonitis		2
Parametritis		4
Ruptured uterus, shock, pituitary necrosis		1

TABLE III. PRINCIPAL INDICATIONS FOR CESAREAN SECTION

INDICATION	BAPTIST HOSP. (SECTION RATE 7%)	CHARITY HOSP. SERIES WITHOUT AUREOMYCIN (SECTION RATE 3.71%)	CHARITY HOSP. SERIES WITHOUT PROPHYLACTIC DRUG (SECTION RATE 3.41%)	CHARITY HOSP. SERIES WITH AUREOMYCIN (SECTION RATE 3.99%)
Repeat	37%	43%	28%	60%
Disproportion	25%	24%	30%	19%
Placenta previa	12%	7%	14%	6%
Placental separation	5%	4%	4%	5%
Toxemia	1%	4%	12%	5%
Inertia	8%	4%	6%	2%
Others	12%	14%	6%	3%

The section rates and principal indications are noted in Table III. The higher section rate in private cases results in a higher percentage of favorable cases as regards infection. It was evident that inertia was associated with conditions favoring infection and tended toward a higher morbidity. The other major indications listed did not per se exhibit a definite effect.

TYPE IV. TYPES OF OPERATIONS PERFORMED

	BAPTIST HOSP. SERIES	CHARITY HOSP. SERIES WITHOUT AUREOMYCIN	CHARITY HOSP. SERIES WITHOUT PROPHYLACTIC DRUG	CHARITY HOSP. SERIES WITH AUREOMYCIN
Classical	6%	4%	10%	2%
Lower segment	90%	83%	74%	66%
Extraperitoneal	4%	3%	14%	4%
Section hysterectomy	0%	10%	2%	28%

The types of operations are noted in Table IV. The extraperitoneal operations in the Baptist Hospital series were performed by one operator, who used this procedure routinely. The extraperitoneal approach was used in the Charity cases for the most part as indicated by infection or marked contamination. It appeared to decrease morbidity particularly in the series without prophylactic drugs. Of the 28 hysterectomies done in the series with aureomycin, none were primarily done because of infection.

Of the deaths, none were due to infection. No mother died in the Baptist Hospital series or in the L. S. U. Department of Obstetrics control study. In the Tulane Department of Obstetrics series without aureomycin 2 deaths occurred. One patient died of a pulmonary embolus while the other died with pituitary necrosis secondary to shock of rupture of the uterus. Three of the mothers receiving aureomycin died, one because of the administration of incompatible blood, the second from irreversible shock of complete placental abruption in spite of massive transfusions and hysterectomy, and the third from lower nephron nephrosis secondary to shock associated with hypertensive cardiovascular disease, pre-eclampsia, postoperative bleeding, and large transfusions.

Comment

The clinical opinion of the members of the nursing staff and of the resident and visiting obstetricians of the Tulane Obstetrical Service at Charity Hospital, who have worked with patients before and after the use of aureomycin, is that aureomycin-treated patients have a better convalescence as regards eating, attitude, emunctory functions, and ambulation. The drug, when properly administered, has been free of undesirable effects. In the amounts used, thrombosis of veins has not been troublesome. The only gastrointestinal upset encountered was nausea when administration was too rapid. Following intravenous administration diarrhea was not noted.

Conclusions

1. Study of morbidity following cesarean section involves consideration of many variable factors.

2. Statistical proof of the influence of a single variable is not possible since other variables cannot be controlled.

3. Evidence to substantiate opinions is submitted.

4. Vaginal bacterial flora (infectivity) appears to be an important factor. In patients with poor vaginal hygiene, likelihood of infection is increased and preventive measures should include prophylactic administration of agents effective against the common pathogens.

5. Prophylactic administration of antibacterial agents during labor when infection is anticipated due to the spread of bacteria is commonly practiced and appears justified.

6. Prophylactic administration at time of section and thereafter when infection is likely is commonly practiced and appears justified.

7. Effective antibacterial therapeusis has increased the safety of leaving an infected uterus in situ and decreased the need of extraperitoneal approach; however, decision as to type of section for each patient should be reached after consideration of all factors involved.

8. Improvement in total obstetric care by patients and by physicians has reduced the frequency of situations favorable to infection and is probably the

primary cause of reduction in mortality and morbidity, rather than effectiveness of modern antibiotics.

9. It is our impression that aureomycin is the best single prophylactic antibacterial agent evaluated on the Tulane Obstetrical Service as of April, 1951.

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1430 TULANE AVENUE

UTERINE MALFORMATIONS IN THE MANAGEMENT OF STERILITY AND INFERTILITY

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THE detection of congenital abnormalities of the female genital tract is one of the most important accomplishments in the study of sterility, and the uterotubogram offers very valuable aid in their discovery. There is no other way which is equally as simple and effective in determining the nature and the degree of uterine abnormalities. Apparently, there are two schools of sterility investigators: those who adhere to the teachings of Rubin[1] who claimed, some years ago, that the insufflation of the tubes with air or gas would offer complete information as to the functional state of the uterus and tubes and who would like to see the use of iodized oil stopped; and those who believe that insufficient evidence is gained from tubal insufflation but that the x-ray picture offers a much greater aid in obtaining information as to the anatomical structure of the organs connected with the reception and development of the fertilized egg. The French[3, 4, 5] have been the protagonists of this manner of study, and were the first[6] to use hysterosalpingography routinely in gynecological diagnosis and sterility investigation. But even Rubin himself[2] concedes that hysterosalpingography is the only way of detecting congenital uterine malformations. The recent American literature contains several references,[7-12] where large series of hysterosalpingograms have been done and, provided certain precautionary measures have been observed, few untoward effects have been noticed. Karshmer and Stein[13] even point out that the danger of air embolism following tubal insufflation is greater than the one from oil embolism following uterotubography, and thus declare the latter procedure as safer.

The uterine malformations can be appreciated only if one understands the embryology of the female genital tract. The tubes as well as the uterus originate from the Müllerian ducts which in later embryonic life are supposed to fuse. If this fusion has either been incomplete or not taken place at all, one will get the different types of split uterus. On the other hand, if there is a suppression of one entire Müllerian duct on either side, the type of organ called uterus unicornis will result. Jarcho,[14] in his classical paper, quotes Kaufmann's classification of the different deformities of the uterus and it is this classification that will be adhered to in this paper.

Uterus Bicornis Unicollis

CASE 1.—Mrs. R. M., 27 years old, nulligravida, was referred because of involuntary sterility* of three years' duration. Her previous medical and surgical history had been ir-

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*In using the terms "sterility" and "infertility," the definition, as given by Paul Bernhard[15a] is adopted: Sterility = inability to conceive, impotentia concipiendi; infertility = inability to carry the conceived pregnancy to term, impotentia gestandi.

relevant. She had her first catamenia at the age of 17 years, but had never menstruated regularly since. The intervals between periods lasted from 39 to 71 days, and she menstruated 6 to 7 days. For the past two years, she complained of dysmenorrhea and oligomenorrhea. The patient had never had any investigation or treatment of her sterility. Physical examination showed the patient to be 64¼ inches tall, weighing 111 pounds. She presented an infantile habitus with underdeveloped breasts and scarce axillary and pubic hair. Pelvic examination showed the cervix to be small, nulliparous, with small erosion and slight endocervicitis. The uterus showed a somewhat broadened fundus, anteflexed, freely mobile. Adnexa were not felt. An endometrial biopsy was taken which showed that the patient had an anovulatory menstrual cycle. In March, 1951, a hysterosalpingogram was done using 8 c.c. of Lipiodol. The fractional method of injection was employed. No difficulty was encountered in introducing Jarcho's cannula. As can be seen from Fig. 1, the cannula was introduced into the left horn of the uterus, yet enough reflux was present to fill both horns adequately. The films show a uterus bicornis unicollis with a short cervix and two fairly well-developed horns. The left side, however, seems to be larger than the right one. Both horns run in a straight line for about ½ of their length and then they show an angulation of about 90 degrees. The left tube is well developed and shows minimal spilling effect. There are no signs of the right tube at all (Fig. 2). It cannot be determined whether the tube is occluded at the uterine end, or whether it is congenitally absent. Another film was taken ½ hour after the removal of the instruments which showed small amounts of dye in the peritoneal cavity.
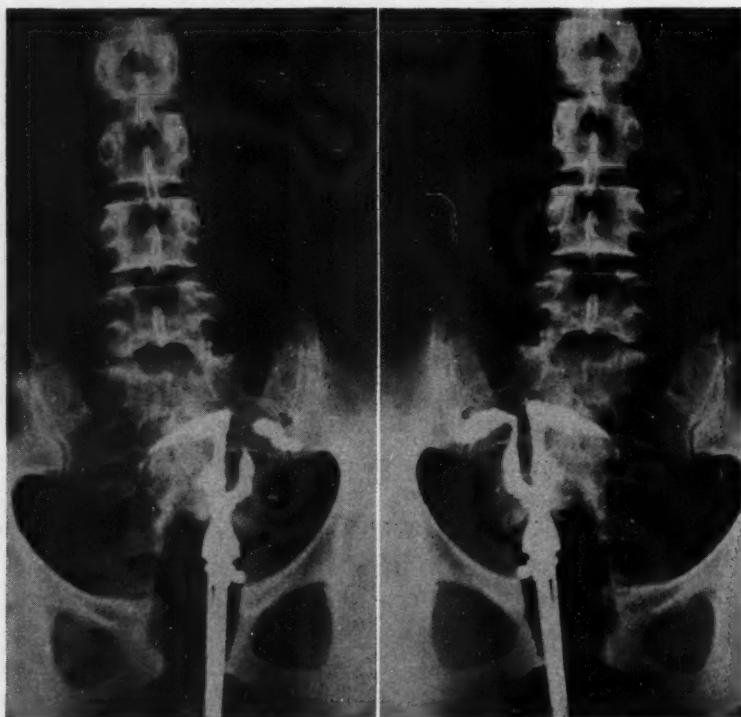

Fig. 1.   Fig. 2.

Fig. 1 (Case 1).—Uterus bicornis unicollis after injection of 6 c.c. Lipiodol. Left tube patent, right tube occluded at uterine end.

Fig. 2 (Case 1).—Uterus bicornis unicollis after injection of 8 c.c. Lipiodol.

In advising this patient as to further therapy it was considered best to leave her untreated. In case of pregnancy her chances of having a spontaneous abortion were regarded as too great, and particularly the danger of a spontaneous rupture of the uterus was thought to be

too much of a risk, if the pregnancy should occur in the less developed horn. This patient presents an interesting problem as to the management of this abnormality. It is fairly certain that the reason why this patient did not get pregnant was her anovulatory failure, and not her uterine abnormality. It appears, and Jarcho[14] seems to be of the same opinion, that the abnormality "per se" is not a reason for sterility, provided that the endometrium shows an adequate progestational response. However, the question arises what is going to happen to such patients in future pregnancies? Stander[16] has made a study of these cases and he claims that about half of them go to term, whereas the other half show repeated abortions or even rupture of the uterus during pregnancy, if the wall of one horn is not developed enough to carry a gestation to term. However, one does not know in advance which course a patient is going to take and therefore it was thought better in this particular case to leave the woman untreated. Whether one would have been able to correct the anovulatory failure is a matter of conjecture. The interesting part, however, is that even after the hysterosalpingogram had discovered the uterine malformation and the patient was re-examined, the evidence found on pelvic examination was insufficient to determine that this woman had a uterine malformation, and that has been true in other cases of uterus bicornis unicollis. It depends upon the depth of the indentation at the fundus, whether the abnormality can be recognized on pelvic examination.

Naturally, the uterus didelphys is usually diagnosed by speculum examination whereas the uterus bicornis unicollis is only rarely diagnosed by bimanual palpation, and therefore the hysterosalpingogram is diagnostic for this abnormality.

Fig. 3 (Case 2).—Uterus bicornis unicollis with small filling defect in right horn (submucous myoma or endometrial polyp?). Patient had five spontaneous abortions.

CASE 2.—Mrs. M. P. was a 26-year-old woman who came to this country as a displaced person in 1950. She had been married for six years and practiced coitus interruptus during the first year of her marriage. She had had five spontaneous abortions ranging from six weeks to three and one-half months' duration, and each abortion was followed by a curettage because of retained secundines. The last curettage was done in this country after a spontaneous abortion at three and one-half months, yet nothing peculiar was noted by the operating

surgeon. Physical and pelvic examinations did not show anything abnormal except a mod-
erate erosion of the cervix with endocervicitis. A hysterosalpingogram was also done on this
patient using the fractional method of injection with Lipiodol (Fig. 3). The cervix is of
normal length, but shows some saw-tooth appearance within the cervical canal. The uterus
consists of two horns: a long but slender right one and a short stubby left horn. In the
right horn, there is a small persistent filling defect indicating either an endometrial polyp
or a small submucous myoma. Both tubes are patent with spilling of oil into the peritoneal
cavity. The right tube appears somewhat tortuous.

   Diagnosis: Chronic endocervicitis, uterus bicornis unicollis with submucous myoma (?).

   Although the anatomical structure of this uterus closely resembles that of the first case,
the clinical course has been entirely different. Whereas the first woman has been unable to
get pregnant at all (for other reasons than her uterine abnormality), this woman has be-
come a habitual aborter. This therefore proves Jarcho's[14] observation that uterus bicornis
unicollis alone cannot be held responsible for sterility. These patients exhibit infertility, be-
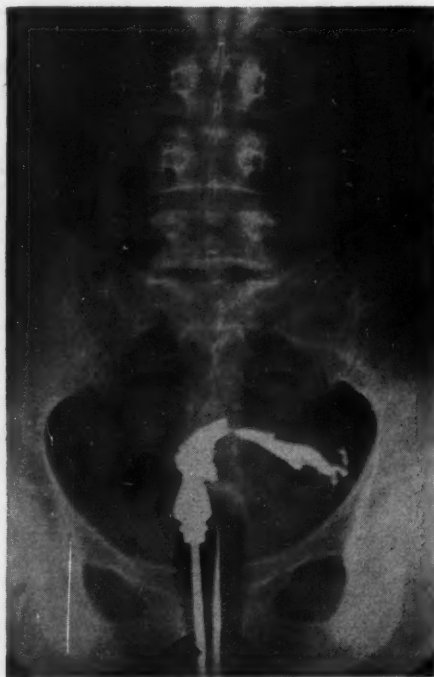cause of the underdevelopment of the individual uterine horns.

Fig. 4 (Case 3).—Uterus unicornis. Note the different filling defects, probably due to myomas.

Uterus Unicornis

   CASE 3.—Mrs. G. S., aged 39 years, has been married for two years, and has never been
pregnant. She has always been in good health. Menarche was at age 13, with a normal 28-
day cycle, lasting three days. There was no recent change in her menses. Her pelvic examina-
tion showed a marked dextroposition of the uterus which was not enlarged and was moder-
ately mobile. Her sterility work-up was entirely normal. The Hühner test was normal. The
endometrial biopsy showed a good luteal phase. In doing the salpingogram, great difficulty
was encountered in introducing the cannula into the uterine cavity. It took considerable
probing for about 15 minutes before the opening was found which lay to the right and
posteriorly. The cervical canal felt rather roomy, and the cannula could be freely moved
to and fro in the cervical canal. It also was noted that the endocervix showed marked
roughening.

Hysterosalpingography revealed the cervical canal unusually dilated, uneven, with stenosis of the internal os. The uterus was in marked dextroposition, the uterine cavity elongated with persistent filling defects on either side (Fig. 4). The form and shape of the uterus were consistent with that of one single horn, at the end of which one tube was situated, which was patent and allowed a free escape of oil. After twenty-four hours the oil was evenly distributed throughout the pelvis.

Diagnosis: Cervicitis with sac formation of the cervical canal, uterus unicornis with patent tube, myomas of the uterus.

According to Jarcho[14] this is a fairly rare uterine abnormality. Less than 100 cases of this malformation have been described in the literature. He himself adds two of his own, both of which presented sterility problems. The first one was preoperatively diagnosed as fibromyoma of the uterus and cervical polyp, and a subtotal hysterectomy was performed. Only after opening the removed uterus was the proper diagnosis established. The second patient presented involuntary sterility of four years' duration; a hysterosalpingogram disclosed the presence of a uterus unicornis.

Fig. 5 (Case 4).—Uterus arcuatus or cordiformis. Uterus is hypoplastic. Patient had oligo- and hypomenorrhea, with anovulatory failure.

This patient did not conceive but I am inclined to believe that sterility was due to the cervical malformation and not to the existence of a uterus unicornis.

The sac formation of the cervical canal has been observed previously by Schultze,[17a] who demonstrated two cases of marked uterine hypoplasia with a similar dilatation of the cervical canal. Schultze is of the opinion that this in itself is a congenital malformation of the cervix which sometimes is also observed independent of any abnormality of the corpus. One can assume that the extreme difficulty I had in finding the entrance to the uterine cavity must also be encountered by the sperm and the logical treatment for the condition would have been a homologous artificial insemination, since the husband's sperm count was of high quality. However, the couple was not favorably inclined to this procedure. Since the publication of Jarcho's paper, only one other case of uterus unicornis has been reported in the literature.[18]

Uterus Arcuatus

CASE 4.—Mrs. F. B., aged 19 years, married for one year, had never been pregnant. Her medical history was irrelevant, she had had no operations. Menarche was at age 14, a 25-day cycle, lasting for 5 days, with moderate flow. The patient had had periods of oligo- and hypomenorrhea.

Hysterosalpingogram was done, using 8 c.c. of Lipiodol which were injected by the fractional method. The picture showed a very marked spasm of the internal os. The uterine cavity was very small with a marked indentation at the middle of the fundus (Fig. 5). Both tubes were patent.

Diagnosis: Spastic internal os, hypoplastic uterus arcuatus.

This is the mildest form of uterine malformation, where only a very small part of the uterine cavity is divided by a septum, which gives it a typical heart-shaped form, whence this abnormality gets its alternate name, uterus cordiformis. The differentiation of uterus subseptus and arcuatus sometimes may be difficult, since the distinguishing characteristics may be extremely fine. The prognosis as to conception in these cases is fairly favorable. The reason for sterility of this patient is that repeated endometrial biopsies showed her to have an anovulatory cycle.

Uterus Didelphys

CASE 5.—Mrs. F. C., 33 years old, was first seen in the Prenatal Clinic on Jan. 13, 1949. At that time, she gave the history that in June, 1947, she had a normal spontaneous delivery of an illegitimate baby who was born at home and attended by a midwife. Nothing else is known about this confinement.

Second Pregnancy: Her last menstrual period was unknown. On her first visit (Jan. 13, 1949) she complained of occasional vaginal bleeding. The information that could be gotten from the patient was not too reliable, since the patient herself had an extremely low I.Q. A Wassermann test taken on the day of admission was 4 plus positive and she was given the usual ten-day penicillin treatment. Her blood type was O, Rh positive. On admission, the examining attending physician made the following note: ''Slight vaginal bleeding, Friedman test positive. Pelvic examination: There is a vaginal septum, complete and intact, making a larger vaginal space on the right side and a similar one on the left. On the right side, the cervix and the fundus can be palpated; the latter is not enlarged. On the left side, a cervix is likewise felt, but the fundus cannot definitely be made out. Speculum passed on both sides of the septum and a cervix seen on both sides. The spotting seems to be from the *left* cervix. From the appearance of the two cervices, I believe that the previous birth had occurred from the *right* side and that also the present pregnancy is located in the *right* uterus.''

Diagnosis: Uterus didelphys with pregnancy in the right horn. Patient was placed on stilbestrol and was re-examined at frequent intervals. She had slight vaginal bleeding off and on. On March 24, 1949, the examining physician noted: ''Patient felt life last week, fundus up to the umbilicus, no bleeding.''

She then was admitted to the hospital on May 17, 1949, with the history that she had bled profusely at home and had passed several big clots in the toilet which were not saved. Vaginal examination: There was a mass the size of a small orange in the region of the right adnexa. The cervix was patulous with placental tissue hanging out from the cervix. The placental tissue was then removed with a sponge stick and the uterus packed. Bleeding stopped immediately and the packing was removed after twelve hours. The patient was discharged in good condition on May 19, 1949. On discharge from the hospital she was instructed to return to the Gynecological Clinic so that she could be scheduled for a vaginal plastic (removal of the septum). However, the patient never returned until she was pregnant again.

Third Pregnancy: The patient returned on Dec. 8, 1949, stating that her last menstrual period had been on Sept. 7, 1949, which made her estimated date of confinement on June 14, 1950. Her Wassermann at that time was still 4 plus positive; therefore, she received a second ten-day penicillin treatment of 6,00,000 units. She had an uneventful pregnancy and went

into labor spontaneously at 10:00 P.M., June 5, 1950, and was delivered at 4:27 A.M., June 7, 1950. It was noted that her contractions were of rather poor quality. Delivery occurred from the *left* side of the vagina and the septum tore during the delivery. The laceration was repaired by the intern and, when the attending came in the next morning, he noticed that the intern had sewed up the septum back in its old place. The attending then took out the sutures, resected the septum, and repaired the vaginal wall. He noted at that time that the left cervix was soft, easily admitted two fingers, and the fundus was the size of a small grapefruit. The right cervix was patulous but the fundus was not enlarged. The patient made an uneventful recovery and was discharged from the hospital on June 11, 1950.

Fourth Pregnancy: The patient returned to the Prenatal Clinic on March 8, 1951, stating that her last menstrual period had been in July, 1950, about one month after her last baby was born. At the time of admission, she was estimated to be about 32 weeks pregnant. She had a completely uneventful pregnancy and from examination it was noted that she was pregnant in the *left* horn. She went into labor spontaneously at 1:00 P.M., May 7, 1951, and had a full-term, spontaneous delivery after 4 hours and 23 minutes of labor. This delivery was supervised by the writer and it was noted that delivery occurred from the *left* horn of the uterus. The days postpartum were uneventful and the patient was discharged on May 12, 1951.

In recapitulating this case, it is definitely known that the patient had a spontaneous delivery in 1947 from the right horn, a spontaneous abortion in 1949 also from the right horn, and two spontaneous deliveries in 1950 and 1951 from the left horn. This patient with a uterus didelphys has been observed through four pregnancies and apparently has two normally functioning horns.

General Considerations

Incidence.—The incidence of uterine malformations is very difficult to evaluate. Since the diagnosis is very often missed on physical examination, and sometimes made only at the operating table or in the pathological laboratory, statistics must be by necessity unreliable. Schultze,[17b] whose book is based upon 2,000 uterotubograms, encountered 50 cases within one year. Bernhard[15b] quotes Hörmann who found among 2,000 hysterosalpingographies on women with primary and secondary sterility, 41 cases equaling 2 per cent with proved split uterus; of those, 18 were cases of uterus subseptus, 15 of uterus bicornis, and 8 of semiuterus unicornis. Taylor[19] estimates the incidence of uterine malformations of one in 1,500 obstetric, and about one in 2,000 gynecologic cases.

It appears to this writer that these figures are by far too low. Since most of the cases give no symptoms which would lead one to look for a uterine malformation, it is extremely difficult to make up any statistics, unless one has done as many uterotubograms (4,800) as Robins.[10] My own series of hysterosalpingograms comprises only a small fraction of that number, and yet the first 4 cases described were encountered within a period of about 18 months. Thus, it appears that routine contrast studies with Lipiodol in all sterility cases will bring out a greater number of these abnormalities.

Jurgens[20] described 7 patients with uterine anomalies of whom only one gave an abnormal Rubin test, thus confirming the importance of x-ray studies. I also feel that the foreign body reaction of the peritoneum due to the Lipiodol (Rubin[21]) has been somewhat exaggerated. However, the following points of caution should always be exercised: (1) Hysterosalpingograms should not be taken if a woman is bleeding (danger of injecting oil into open uterine sinuses); they should not be done until about 10 to 12 days after onset of menstruation. (2) Hysterosalpingography should not be performed after a dilatation and curettage. The woman should have had at least two normal periods. (3) The oil should be injected under fluoroscopic control and a manometer, such as has been described by Robins,[10] should be interposed between the syringe and the uterine cannula. If the oil is warmed sufficiently

before injection, the pressure need never exceed 200 mm. Hg. If these points are strictly observed, the procedure is certainly harmless and can be done routinely in the office.

I fully well realize all the arguments which have been brought forth against hysterosalpingography, yet I have been fortunate not to have had any untoward effects. Only recently, a case of oil embolism was reported by Karshmer and Stein[13] which luckily had a happy ending. Marshak, Poole, and Goldberger[9] also recently reported an analysis of 2,500 hysterosalpingographies: in the 38 cases where dye had entered the uterine vessels, water-soluble media were used. In no cases, where Lipiodol was used, did this accident occur.

Uterine Malformations Affecting Sterility and Infertility

Jarcho[14] seems to feel that conception is not materially altered in women with malformed uteri, whereas Siegler[22] seems to be of the opposite opinion. Bernhard[14b] quotes Philipp who found in 46 women with some form of double uterus that 20 showed primary sterility (43.5 per cent), whereas 26 became pregnant (56.5 per cent) one or more times, resulting in 64 gestations. These 64 pregnancies ended in 16 full-term deliveries, 10 premature labors, and 38 spontaneous abortions. According to his statistics the women with uterus didelphys showed the greatest percentage of primary sterility (50 per cent), those with uterus septus 45.7 per cent, and those with uterus bicornis unicollis showed a primary sterility rate of only 20 per cent. Schauffler[24] who presents 11 cases in 2 of which there was ''difficulty in becoming pregnant,'' believes that ''fertility is definitely not impaired. In fact, one is almost tempted to infer that fertility and the sex urge are distributed among these women in the same generous ratio as their organic sex equipment.''

In my own cases, three out of five women showed a primary sterility, whereas one (Case 2) exhibited infertility, and one (Case 5) had 3 full-term spontaneous deliveries. However, I believe that sterility in those cases was due not to the uterine malformation, but to other causes, such as cervical malformation or anovulatory failure (hypo- and oligomenorrhea). This phenomenon is encountered frequently enough, as I brought out in a previous paper,[25] and, thus, may be blamed for the primary sterility.

However, there appears to be a consensus that the miscarriage rate runs proportionately high in these patients. Schauffler,[24] whose 11 women had a total of 32 pregnancies, mentions 17 abortions (53 per cent). Jarcho[14] presents 18 patients of whom 6 were sterile, 5 patients had 10 living children and one stillbirth, whereas 4 women had 8 spontaneous abortions (44 per cent). Taylor[19] mentions 25 per cent, whereas Bernhard's[15c] figures are even higher. He presents a table comprising 87 cases of malformed uteri; 52 of these patients (59.8 per cent) had 122 pregnancies. There were 74 abortions in this series, which is 60.6 per cent of all pregnancies which occurred. Bernhard[15c] furthermore quotes Bertlich who found among 60 cases of uterus bicornis 43 per cent of spontaneous termination of pregnancy before the twentieth week.

This last statement infers that the termination of pregnancy in a split uterus does not necessarily have to take place by way of a spontaneous abortion. This occurrence will prevail, if both horns are equally well developed; if, however, there is one rudimentary horn with no or insufficient connection to the cervix, the impregnation of the underdeveloped horn may present the clinical picture of an ectopic pregnancy. Eastman[26] mentions several references where such a catastrophe is described; yet, in the majority of cases, the diagnosis was made only after the abdomen had been opened. Amputation of the pregnant horn is the only alternative in the treatment of these patients. Recently, Hoerner and co-workers[27] described a similar case.

Summary and Conclusions

1. Routine hysterosalpingography is required in all sterility and infertility studies, in order to detect uterine malformations, provided that certain precautionary measures are observed.

2. Two cases of uterus bicornis unicollis, one case of each, uterus unicornis, uterus arcuatus, and uterus didelphys with two functioning horns are presented.

3. The incidence of uterine malformations appears to be greater than has heretofore been realized.

4. None of the abnormalities is a cause of sterility per se; usually other factors are responsible for the failure of these women to conceive.

5. Anatomical abnormalities of the uterus predispose to spontaneous, and sometimes to habitual, abortions, thus causing infertility.

6. Impregnation of a rudimentary horn in a split uterus may simulate ectopic pregnancy.

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ADENOCARCINOMA OF THE ENDOMETRIUM, A CLINICOPATHOLOGIC STUDY*

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THERE is a growing conviction that the cause of cancer will be found in abnormal intracellular metabolism. It is a widely accepted fact that there are genetic as well as extrachromosomal factors involved, but there is a wide divergence of opinion as to the relative importance of either of these factors in the subsequent histogenesis of a neoplasm.[1]

The purpose of this paper is to survey the individual who develops adenocarcinoma of the endometrium. A study is made of inherited and acquired characteristics which might possibly provide additional information concerning the genesis of this particular type of tumor. Previous similar studies have demonstrated a higher incidence of endometrial carcinoma in the postmenopausal nullipara of comparatively large stature who is also overweight.[2,3] In addition, the patient frequently presents a history of a menorrhagic climacteric or delayed menopause.[4] Evidence is increasing that such individuals have an abnormal estrogen metabolism although the precise nature of this dysfunction is as yet unknown.[5,6]

Material

During the period Jan. 1, 1926, through Dec. 31, 1950, there were 10,160 gynecological patients discharged from The Pittsburgh Hospital. In this number, adenocarcinoma of the endometrium was diagnosed in 85 instances. For the purpose of this survey the clinical record, pathological report, and all available histological slides of each case were reviewed.

Results

In order to maintain clarity, the results of this investigation are divided into two sections. Section I concerns a statistical analysis of the survey. Section II contains the information provided by the pathological review.

Section I.—This is an admittedly small series of cases of adenocarcinoma of the endometrium and the statistical analysis must be interpreted with this fact in mind.

The data compiled reveal that the incidence of this neoplasm among gynecological patients admitted to a general hospital over a twenty-five year period was 8.3 per thousand. Fig. 1 demonstrates that there was no significant alteration in the incidence during the period studied.

The average age of the patients when the diagnosis was made was 55.6 years and Fig. 2 demonstrates that almost 30 per cent of cases developed between the ages of 55 and 59 years and approximately 60 per cent developed between 50 and 64 years.

Cessation of the menses occurred at the average age of 48.9 years which is approximately one year later than the generally accepted age of the menopause among the female population. A significant fact illustrated by Fig. 3 is that 44.6 per cent reached the menopause between 50 and 54 years.

The climacteric was complicated by menometrorrhagia in 35 per cent of these individuals. Analysis of the social history revealed that four out of five of the patients had been married but 51.6 per cent of these did not conceive. Among those who did conceive there were 133 pregnancies of which 37, or 28 per cent, terminated in abortion. Accurate weights of the individuals were not available in all instances but 40 per cent were considered obese on clinical examination. An estimation of the incidence of vascular hypertension proved difficult because there is no unanimity of opinion as to what constitutes a normal reading for any one of either sex of definite age, stature, and weight.
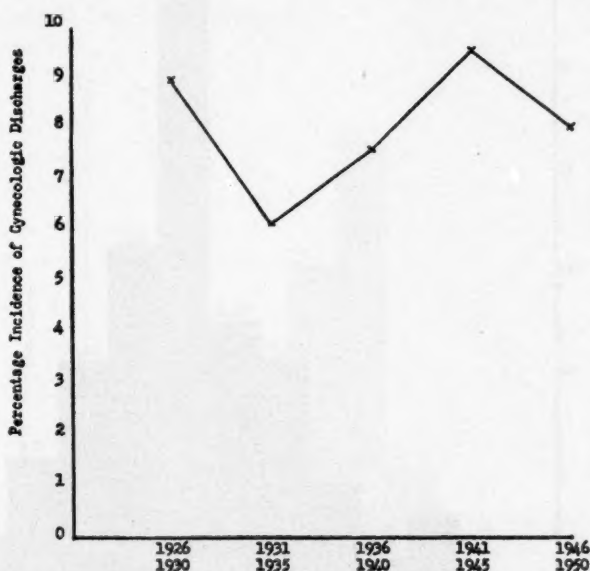
Fig. 1.—Incidence of adenocarcinoma of the endometrium by five-year periods, 1926-1950.

Section II.—The second portion of this survey was hampered by some insurmountable difficulties because of the varying trend of treatment of this neoplasm as well as the ravages of time.

Completed pathological reports, gross and microscopic, of the uterine and ovarian tissues removed were available in 57 cases. For the purposes of this survey the presence of myomas, measurements of the uterus and ovaries, as well as the existence of ovarian cysts were recorded. Microscopic review of the histological sections of these tissues was possible in only 47 instances and this was done in the light of recent writings by Hertig,[7] Novak,[8] and Tannhauser.[9]

Examination of the endometrium revealed that hyperplasia existed in 36 per cent, endometrial polyps in 9 per cent. Acanthomatous changes were apparent in 7 per cent of the cases.

Inspired by the studies of Tannhauser on the myometrial changes in cases of adenocarcinoma of the uterus, we reviewed our material and attempted to make a similar comparison between the size of the malignant and nonmalignant uteri in the same age group. He states that the largest postmenopausal, nonmalignant, nonleiomyomatous uterus he encountered in his investigation measured 12.5 by 3 by 2.5 cm. We used the product of these figures as a volumetric

index of the largest possible normal postmenopausal uterus. Analysis of the data compiled on malignant, nonleiomyomatous uteri revealed that in the decade between 50 and 60 years the malignant uterus had an average volumetric index of twice the normal. This bears out Tannhauser's observation that the increased size of the uterus is not alone caused by the size of the neoplasm.

Microscopic examination of the myometrium revealed it to be of the premenopausal type in 58 per cent of the sections examined. Adenomyosis was encountered in 9 per cent and leiomyomas in 49 per cent. Critical examination of the architecture and component cell morphology of the leiomyomas revealed that in 43 per cent there was no evidence of the degeneration to be expected with the normal postmenopausal decrease in circulating estrogens.
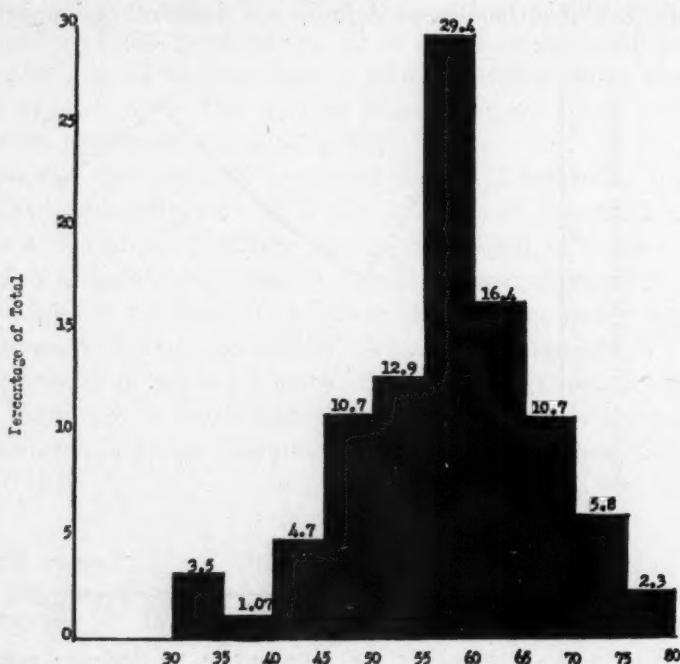

Fig. 2.—Age incidence of diagnosis of adenocarcinoma of endometrium.

The ovarian pathology concomitant with endometrial carcinoma was reviewed and the data compiled were based on the writing of Hertig in this field. Postmenopausal activity of the ovarian stroma was encountered in 55 per cent and retention cysts in 47 per cent, active endometriosis in 4 per cent, and one granulosa-cell tumor was found.

Comment

The authors realize that the number of malignancies in this series is too small to permit sharp breakdown of the statistics compiled or to draw therefrom far-reaching conclusions. However, some facts have been demonstrated that warrant further discussion.

The prevalence of diabetes mellitus among females of the general population varies considerably from one author to another. There have been no large-scale observations in a population to determine what the true prevalence of the disease would be. We considered the findings of Wilkerson and Kroll[10] during a diagnostic survey of a small community to offer the least possible error in com-

parison. Results of that survey revealed that the incidence of diabetes mellitus in women aged 45 to 54 years was 4 per cent, and 6 per cent for the next decade. In this small series of uterine malignancies the incidence of diabetes for the same age groups was 14 per cent and 18 per cent, respectively, or approximately a threefold increase. Although the precise etiology of diabetes is just as obscure as that of carcinoma, it is believed that the onset of diabetes depends upon metabolic disturbances.[11] Such disturbances are undoubtedly related to the endocrine secretions. The exact nature of the relationship between the endocrines of the anterior pituitary and those of the pancreas and adrenal remains unsolved but that such relationship exists is demonstrated by considerable clinical evidence and animal experimentation. Excessive anterior pituitary secretion can result in exhaustion and secondary changes in the beta cells of the Islands of Langerhans.[12] That the anterior lobe of the pituitary in the postmenopausal woman is hyperactive in the production and release of its secretions has been demonstrated by Sevringhaus.[13]
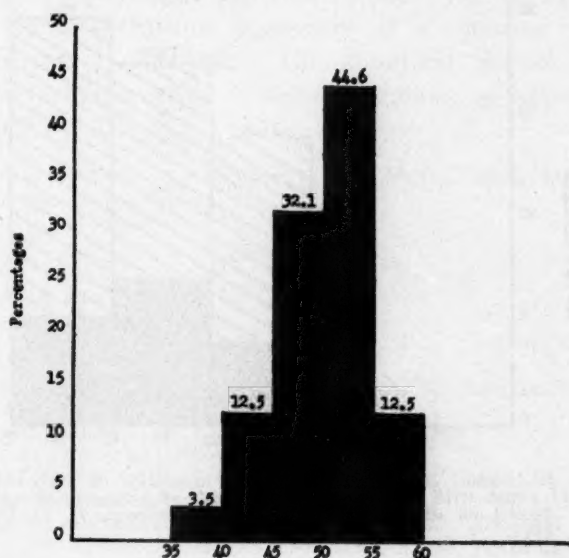

Fig. 3.—Age at menopause in cases of adenocarcinoma of endometrium.

Another significant finding is the apparent increased incidence of vascular hypertension in this group. As noted above, the estimation of normal blood pressure for any one group is difficult because no exact definition of the limits of normal pressure exists. However, the work of Master, Dublin, and Marks[14] reveals that blood pressure readings usually considered abnormal may be more frequent in the older age groups than some so-called normal readings. The tables of these authors have been accurately reproduced and the various corrections added. We superimposed the blood pressure readings in these cases of carcinoma.

Study of this comparison reveals that 25 per cent of these patients are still borderline or positive hypertensive patients when corrected for age, weight, and the normal deviation from the mean. We feel that this incidence probably represents a truer picture of the extent of hypertension in the group studied than any fixed reading of the sphygmomanometer but whatever the definition employed the incidence of vascular hypertension in our survey is considerably greater than would be expected for women of the same age group in the general population.

The theory of the pituitary origin of diabetes mellitus and hypertension still lacks confirmation. However, that hypertension, both of the paroxysmal and persistent type, can occur in association with disease of the adrenals has been reported.[15] It is not unreasonable to speculate that excessive anterior pituitary secretion can stimulate the entire adrenal, which in turn possibly initiates pancreatic changes through the action of cortisone and the epinephrine produces vascular alterations simultaneously.

A third significant observation we feel is the occurrence of marked obesity in 41.6 per cent of the cases studied. Since accurate weights were not available, the standard of 10 per cent overweight corrected for age was chosen to make comparison. This undoubtedly underestimates the true proportion. Statistics furnished by the United States Public Health Service[16] reveal that 33 per cent of women between the ages of 50 and 59 years are overweight.
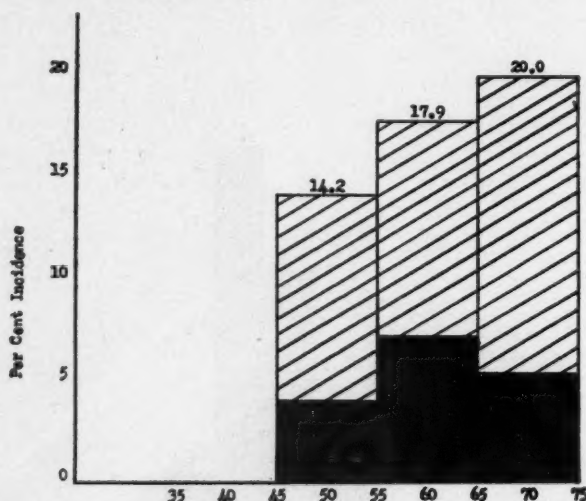

Fig. 4.—Age at diagnosis. Solid black indicates incidence of diabetes mellitus in general female population contrasted with incidence in the cases of adenocarcinoma studied (indicated by cross hatching). Based on diagnostic survey by Wilkerson, H. L. C., and Kroll, L. P.: J. A. M. A. 135: 209, 1947.

Obesity cannot be directly attributed to hypo- or hyperfunction of the endocrine glands.[17] However, dysfunction of these glands can produce changes in the energy metabolism of the body and necessitate a diminished caloric intake if obesity is to be avoided. Corscaden and Gusberg[18] have demonstrated a higher incidence of corpus carcinoma in individuals who are economically secure. The expenditure of energy in these individuals is not in proportion to their caloric intake and as a result they are obese. The causal factors of obesity and diabetes are probably very closely linked and it is possible that booth reflect some underlying imbalance in body metabolism.[19]

There is increasing evidence in support of the theory that the estrogens are one factor responsible for the pathogenesis of adenocarcinoma of the endometrium. This evidence is derived not only from clinical studies but from careful histologic appraisal of tissues known to be influenced by these steroids. Neither the exact motivating force nor the source of the estrogens has yet been positively identified. The endocrine dysfunction does not necessarily originate in the ovaries, for Smith[20] has demonstrated the development of adenocarcinoma of the endometrium in patients who have had a previous bilateral oophorectomy. This would suggest a fault in the metabolism of the adrenal cortex since it is known to be a source of female steroids. However, the authors think, as do

others,[21] that the basic fault exists in the secretions of the anterior lobe of the pituitary. Excessive amounts of these pituitary hormones produce an abnormal activity of the receptor glands. The ovaries and/or adrenals respond by secreting estrogens whose metabolism is not moderated by progesterone. Such a disordered estrogen metabolism can well be the extrachromosomal fault which provokes an abnormal response in chromosomes whose genes possess the hereditary potential of abnormal growth.

Summary

The knowledge gained from this survey confirms the findings of other investigators that adenocarcinoma of the endometrium is most frequently encountered in the sterile or infertile woman between 50 and 60 years of age who has had a slightly delayed menopause. The climacteric was commonly complicated by periods of menorrhagia. Hypertension, obesity, and diabetes mellitus were other disorders which were often associated with the development of this neoplasm. The whole picture is suggestive of a common metabolic disorder created by endocrine dysfunction. The abnormal metabolism provides the extrachromosomal factor essential to the development of carcinoma in the individual predisposed by heredity.

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THE MARSHALL-MARCHETTI OPERATION. A REVIEW*

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IN 1949 Marshall, Marchetti, and Krantz[1] described a new operative approach to the problem of stress incontinence, and reported the results in 50 cases. In December of 1949 Marchetti[2] reported on 12 more women operated upon by him during the preceding 18 months. Since that time there have been no further published reports on this operation.

At the University Hospital in New York City, following the publication of Marshall's article, 11 Marshall-Marchetti operations have been done on which there are adequate follow-up data. Since the cure of stress incontinence is a definite problem, it was thought that a report from an institution not originating the technique might be of interest, as, quoting Mr. Shaw of London in a recent article on this subject,[3] "Operations for the relief of stress incontinence have one factor in common—the originators always claim good results."

Following the work of Kelly,[4] who advocated plicating the vesical sphincter, the recent concepts of the surgery for stress incontinence stem largely from the researches of Kennedy.[5] He developed the principle that scar tissue interferes with the action of the urinary sphincters. It was his impression that the trauma of labor produces submucosal hemorrhages which, in turn, cause the formation of scar tissue, fixing the sphincters so that they cannot function properly. He felt that an involuntary sphincter functions best when circular, without attachments, and when suspended freely in a sling. The sphincter mechanism of the bladder depends on the free action of the internal, involuntary sphincter muscle, supported and enhanced by the voluntary sphincter muscle sling containing levator fibers. Kennedy's operation was designed to free the sphincter muscle from its scar tissue attachment by wide lateral dissection of the urethra.

The next important work in this country was done by Aldridge,[6] who, while in general agreement with the anatomical and physiological principles described by Kennedy, revised an old technique evolved by Stoeckel, and added additional urethral support. He found that, despite careful surgery, with the use of either the Kelly or Kennedy technique, the percentage of failures was between 10 per cent and 20 per cent. In an effort to determine the cause of these failures, he analyzed his own cases and concluded that the following factors were usually involved: (1) urinary infection; (2) destruction of the sphincter blood supply; and (3) probable loss of sphincter nerve supply, although this is difficult to prove. The aim of his operation is twofold: (1) To try to reduce the lumen of the sphincter; (2) to replace the urethra in a normal position beneath the pubic arch, and to reconstruct a proper support for the urethra. These aims he attempts to accomplish by placing a sling of two transverse strips of rectus abdominus fascia at the point where the urethra

and bladder meet. This is the most important spot in the physiology of urination, and it is the area in which the Kelly and Kennedy repairs are often weakest. A further advantage of the Aldridge operation is that the fascial sling compression of the urethra is greatest when intra-abdominal pressure is increased. This is because the lateral attachment of the sling is left in position to be acted upon by the contracting rectus muscles.

Studdiford,[7] after an extensive experience with both the Kennedy and Aldridge operations, in 1946 described another procedure which has been widely used in this country. It is based on the same principle as the Aldridge operation but has certain differences which make it perhaps easier to perform. In this operation a single vertical strip of rectus fascia is used as a vaginal sling. Studdiford points out that, using his technique. one has more fascia to work with, and thus is better able to judge the tension of the fascial sling. Both Aldridge and Studdiford feel that the simpler vaginal type of repair should be done first, and that the more extensive sling operation should be reserved for those cases which are unimproved following vaginal plastic repair.

Since 1946 there have been, by such operators as Millin and Read,[8] several further modifications of the basic techniques of Aldridge and Kennedy, each having the same principles in mind. Williams[9] in 1947 suggested a suprapubic approach, but his operation did not originate the idea of periurethral pubic fixation.

In 1949, Marshall, Marchetti, and Krantz published their article on a new concept of the treatment of stress incontinence. Marshall first conceived his method after treating incontinence following perineal and rectal surgery in both men and women. He found that many of these patients had incontinence and retention, the support of the vesical neck having been destroyed by the very nature of the original surgery. It was also noted that perineal uplift or support would relieve, or at least improve, the incontinence, no matter whether this support was external or internal. A method of lifting the base of the bladder, and raising and angulating the urethra was devised by him. This is accomplished in the space of Retzius by placing four sets of parallel sutures in a line, periurethrally, and through the lateral wall of the urethra, running from near the external meatus to the junction of the urethra and bladder on each side. These sutures are then brought through the periosteum of the vesical surface of the symphysis pubis. Tying of these sutures raises and angulates the urethra under the symphysis. In addition, extra sutures from near the neck of the bladder to the overlying rectus muscles may be placed further to reinforce the urethral elevation. The entire procedure should take less than an hour, barring technical complications.

In order that one may attempt to determine in advance the probable success of the operation, a simple preoperative test has been devised. The bladder is filled with 250 c.c. of saline, and the patient is asked to strain in the prone and standing positions, and the resulting incontinence is observed. Next, a Novocain wheal is formed at the level of the interureteric ridge in the vaginal mucosa. An Allis clamp is placed in this wheal on either side of the urethra. Now, with firm upward pressure on the Allis clamp, the patient again strains in both the prone and upright positions. If the test is positive—that is, if urinary control is improved by such pressure, then one may expect success from the operation. The converse is also true, in that downward pulling on the clamp tends to increase the incontinence in those patients in whom this type of operation is most likely to be successful. Further selection by ruling out chronic urethritis, neurogenic bladder, and psychogenic factors must be performed. To quote Marshall, "It will be pointed out later that some of

our failures can be attributed to poor selection rather than to the operation it-
self which is not designed to cure all types of incontinence." Of the 50 cases
reported, 41 were improved and there were 9 failures. Of the latter 6 were
in poorly selected cases by Marshall's own criteria, and there were 3 in whom
the cause for failure could not be ascertained. In his group only 38 cases
were of proved stress incontinence, and, of these, 26, or 66 per cent, had had
one or more previous attempts at surgical relief without success. There were
no severe postoperative complications. Marshall feels that the operation will
be particularly useful when vaginal operation has been unsuccessful, and when
the preoperative test is positive. Marchetti[2] states that excessive scar forma-
tion makes further attempts at vaginal repair impossible in some cases. In
a recent work, by cystometric tests and cystograms, he attempted to determine
the reason for the success of the operation. He found the cystometric studies
to be of no specific value. The cystograms, however, pointed to an incom-
petent vesical sphincter, not associated with an inadequate vaginal support,
but with a relaxation and descent of the vesical neck. Cystograms taken
following the operation disclosed the bladder neck shadow to be elevated from
a position behind the symphysis to one above the symphysis. Marchetti, in
this series, had modified the original operation by placing sutures entirely
periurethrally. He lists these advantages: (1) simple approach; (2) easy
technique; (3) roomy field of operation; (4) may be combined with laparot-
omy; (5) not contraindicated in elderly patients, or during the childbearing
period; and (6) ideal after previous operative failures. He concludes that
simple elevation and fixation of the vesical outlet and urethra provide a firm
attachment of the sphincter and vesical neck, and that these procedures are
major factors in the maintenance of urinary continence.

Material

The 11 women in the present series have all represented true cases of
stress incontinence. Excluded are instances of neurogenic dysfunction, those
due to surgical trauma, and those cases of "urge incontinence" resulting from
inflammatory conditions of the bladder. Incontinence had persisted from
1 to 25 years in these patients. The degree of incontinence varied from
moderate to severe. In this group of 11, 5 had had one or more previous vagi-
nal operations for stress incontinence. The youngest was 37 years of age, and the
oldest 73. With one exception all of these women were parous, having had
from 1 to 6 vaginal deliveries, but there seemed to be no unusual number of
difficult or instrumental deliveries. In association with the stress incon-
tinence, several had one or more additional gynecological symptoms or com-
plaints.

Of the 11 patients reported upon 3 were clinic patients, and the remaining
8 were private. The operations were performed by 4 attending gynecologists,
and 2 resident gynecologists. As a result of the relatively large group of
operators there were certain slight differences in operative technique. This
was reflected largely in the surgeons' choice of type and size of suture mate-
rial. By and large, however, the technique described by Marshall, Marchetti,
and Krantz was closely followed. The only real modification was used in the
last 4 cases. This is simply anchoring the previously dissected upper urethra
by means of a Babcock clamp held by the assistant. This stabilizes the urethra
which has previously been almost completely mobilized so that one may more
accurately place the sutures. The grasp of the clamp includes the whole diam-
eter of the urethra, and is so light as to produce negligible trauma.

Operative difficulties have been minimal. The only one of consequence
has been occasional excessive bleeding from the veins that form a plexus in the

periurethral and paravesical spaces. This bleeding, if encountered, occurs during the early dissection of the fatty tissue about the urethra. It has been our experience, as it has been that of Marshall, that, although the bleeding may appear to be formidable at the moment, simple pressure will control it promptly. Too much clamping and tying of bleeding points seemed to increase rather than decrease this bleeding.

The postoperative courses have been remarkable by their lack of complications. There was in this group only one case of postoperative hematuria, a condition noted several times in the original series. Urinary retention was present in all for periods of from 2 to 8 days, and its management was varied according to the point of view of the individual surgeon. Some left a retention catheter in for several days, others promptly removed it and used a catheter later at regular intervals. The retention, however, proved to be no more of a problem than it is in a comparable series of anterior wall vaginal plastic repairs. The patients were given prophylactic sulfonamide medication postoperatively, either sulfadiazine or Gantrisin in low dosages. Incisional pain was within expected range. The longest hospital stay was 15 days, the shortest 10 days.

All the patients in this report were operated upon during the past 2 years, the last one 6 months ago. The immediate postoperative results were all successful, each patient leaving the hospital continent. Follow-up data have been obtained in the private cases from their own physicians, and in the clinic cases from the records. All but one had excellent results. Postoperative findings are recorded as positive or negative, or continent or not, as any degree of continence is at best difficult to judge. The single bad result is in a patient who probably represents an error in preoperative selection rather than an operative failure. Much of her symptomatology was psychogenic in origin, and she had numerous complaints besides that of incontinence. She had perfect control for 6 weeks, and there is still no objective evidence of stress incontinence. However, as she states that she is occasionally incontinent, she must be classified as a failure. There was no morbidity, either direct or indirect, in the series.

One must be cautious in drawing any conclusions from this small group, or in attempting to express results on a percentage basis, but the results, so far, compare favorably with those of Marshall, Marchetti, and Krantz, and even better with previous reports of various types of vaginal repairs. Nearly half of these patients had already had vaginal operations ending in failures. Thus one is dealing, at the outset, with a group difficult to cure. In none was an associated cystocele present, and all had a positive preoperative test. As regards these results some further recurrence of incontinence over a more prolonged period of time may occur. Marshall, however, had operated on some of his patients as long as 4 years prior to his publication, so it may be seen that cures have lasted at least that long.

Summary

In conclusion, there were 11 Marshall, Marchetti, and Krantz operations performed at the University Hospital in New York City during the past 2 years. Of these, 10 were successful, one was unsuccessful, and there were no complications of note. The operation is relatively easy. Cases must be carefully selected. Although a welcomed advance, it is, nevertheless, no cure-all. It is felt that the principles of the operation are sound, and that it deserves further and wider use as a worth-while procedure in a field in which success has all too frequently not been attained.

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FURTHER STUDIES ON THE INACTIVATION OF PITRESSIN ANTIDIURETIC EFFECT BY THE BLOOD OF PREGNANT WOMEN*

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THE blood of pregnant women will inactivate the oxytocic, vasopressor, and antidiuretic effect of posterior pituitary extract.[3, 5, 12, 16, 17, 19, 20, 21, 22, 23] The significance of this fact is unknown. Considerable work has been done on the oxytocic and vasopressor aspects of this inactivation phenomenon.[12, 21, 22, 23] With the exception of Dieckmann's[5] work in 1950, very little has been done to investigate this ability of the blood of human pregnancy to inactivate ADH. In view of the altered water and electrolyte metabolism which is associated with pregnancy in general and which is marked in pre-eclampsia-eclampsia, and the demonstrated relationship between the decreased rate of inactivation of circulating ADH and the increased sensitivity of experimental animals to posterior pituitary antidiuretic effect,[2, 6] as well as the apparent role which a decreased rate of inactivation of ADH plays in the abnormal water metabolism of Addison's disease and of liver disease,[2, 11, 18] it would appear that this inactivation of Pitressin antidiuretic effect during pregnancy has potential significance.

The purpose of this paper is to present additional evidence relative to this inactivation of Pitressin antidiuretic effect by the blood of pregnant individuals. These data are based on the study of 110 individuals and employ the new method for evaluating Pitressin antidiuretic effect through the use of human subjects which was reported by Dieckmann and associates in 1950.[5]

The first report relative to the inactivation of posterior pituitary extract by the blood of pregnant women was made by Von Fekete in 1930. At this time, he[19] stated that serum obtained from women in the eighth month of gestation would inactivate posterior pituitary oxytocic effect. In 1935, Schockaert and Lambillon[16] reported the inactivation of pituitary vasopressor effect by serum obtained from pregnant women and they[17] and Dieckmann and Michel[3] independently reported the increased susceptibility of individuals with pre-eclampsia-eclampsia to the vasopressor effect of posterior pituitary extract, and postulated that this phenomenon might be due to an abnormality in the inactivation of this substance.

In 1935, Heller and Urban investigated the in vitro and in vivo inactivation of posterior pituitary antidiuretic effect in the experimental animal, and concluded that the process of inactivation was a dual one of adsorption and enzymatic destruction, and that, of the tissues investigated, liver homogenates possessed the greatest inactivating ability.

Working with experimental animals, Eversole[6] in 1939 demonstrated the in vivo inactivation of ADH, and Birnie,[2] in 1950, demonstrated the presence of a hepatic enzyme system which inactivated ADH. This latter investigator established the fact that conditions such as adrenal insufficiency can alter this system with a resulting decreased rate of inactivation of ADH, and an increased sensitivity of the experimental animal to administered ADH.

In 1950 Dieckmann and associates[5] facilitated the investigation of ADH inactivation by reporting a new and simple method for evaluating Pitressin antidiuretic effect through the use of human subjects. They employed this method in the investigation of 27 individuals, and found that the antidiuretic effect of Pitressin is markedly diminished when this substance is incubated with the blood of pregnant women in the last half of pregnancy, as contrasted with the persistence of the antidiuretic effect when incubated with the blood of nonpregnant individuals.

The means by which the blood of pregnant individuals inactivates Pitressin antidiuretic effect has not been reported. However, Werle[21, 22] in 1941 reported that the inactivation of the oxytocic and vasopressor effects of posterior pituitary extract was a result of enzyme activity occurring in the blood of pregnant women. He investigated the qualitative and quantitative aspects of this inactivation in great detail, and presented evidence to indicate that specific enzymes were concerned with the inactivation of these substances. He reported that this inactivation appeared at two months' gestation, increased gradually to a maximum at the time of delivery, and then gradually declined during the puerperium, reaching prepregnancy levels at about 3 to 4 weeks post partum. In addition, he found that these inactivating substances did not cross the renal or placental barriers. Page[12] in 1946 confirmed these observations in respect to the inactivation of the oxytocic effect by a specific enzyme, and reported no difference in inactivating ability in individuals with pre-eclampsia-eclampsia, as contrasted with normal pregnant individuals. This latter observation was confirmed by Aragon[1] in 1948.

In 1949, Dieckmann[4] employed the Robinson, Power, and Kepler[14] test in investigating the inability of pregnant women to excrete ingested water at the normal nonpregnant rate. He found that 40 per cent of individuals with pre-eclampsia-eclampsia evidenced an Addisonian-like inability to eliminate administered water. This suggests that ADH inactivation may be a factor in pre-eclampsia-eclampsia since evidence indicates that the rate of inactivation of ADH is an important factor in the inability to excrete ingested water at a normal rate which is present in Addison's disease.[2, 7, 13]

The demonstration of large amounts of antidiuretic substances in the urine of pre-eclamptic and eclamptic individuals by Ham,[8] Krieger,[10] Schaffer,[15] and Teel[18] further suggests that inactivation of an antidiuretic substance may play a role in the etiology of pre-eclampsia-eclampsia.

Method

The details of the method employed have been outlined elsewhere.[5] In brief, a water diuresis is established in human subjects by the ingestion of water. Five urine specimens are collected, thirty minutes, sixty minutes, ninety minutes, 120 minutes, and 150 minutes following the start of the test. The test solution which contains 0.04 unit of Parke-Davis Pitressin is injected intravenously following the completion of the 60-minute urine collection, and the changes in urine volume and urinary electrolyte concentrations following this injection permit the evaluation of the antidiuretic effect. In the instances where inactivation studies are carried out, citrated whole blood to which Pitressin has been added is incubated at 38 degrees for one hour, and 10 c.c.

of dilute plasma from this solution are injected intravenously as described. For the most part, gynecological patients who are hospitalized for conditions other than pregnancy, and whose state of recovery is such that they are to be discharged in the twenty-four-hour period subsequent to the test are employed. In a few instances, as an alternative, ten-day postpartum patients are employed. The antidiuretic effect is characterized by a sharp reduction in urinary volume and a marked increase in electrolyte concentration in the 90- or 120-minute urine specimens. It was found that the best criterion for antidiuretic effect was that of increased chloride concentration.

The following method is employed in analyzing the results. The 60-minute urine specimen is used as a basis for comparative calculations. The volume of this specimen expressed in cubic centimeters and its electrolyte concentration, expressed in milligrams per cent, were taken as 100 per cent. This served as a base line and the components of the three subsequent urine specimens were expressed in terms of their base-line volumes and concentrations. For example, if the 60-minute urine collection had a volume of 300 c.c. and a chloride concentration of 18 mg. per cent, and the 90-minute urine collection had a volume of 600 c.c. and a chloride concentration of 9 mg. per cent, the 60-minute urine volume and chloride concentrations were each recorded as 100 per cent and the 90-minute volume and chloride concentrations were recorded as 200 per cent and 50 per cent, respectively.
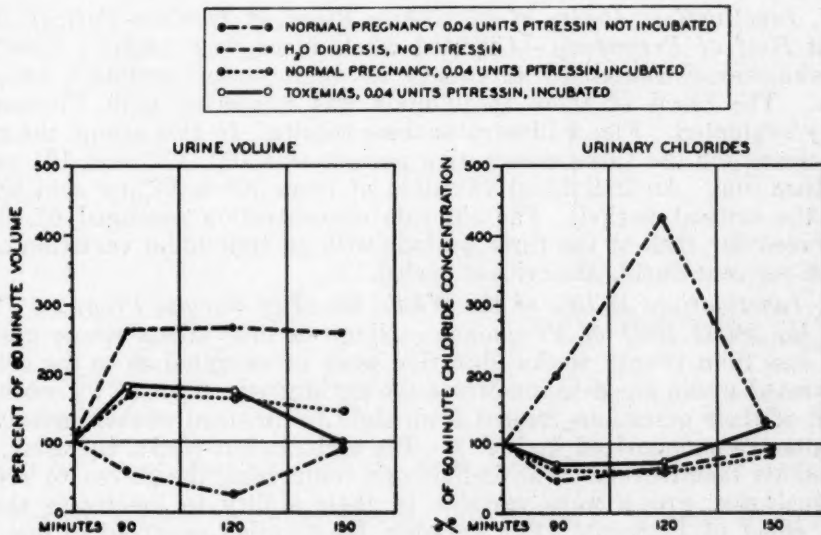

Fig. 1.—Inactivation of Pitressin antidiuretic effect in gestations of twenty or more weeks' duration (mean values).

Results

I. Controls.—A water diuresis alone was established in eleven members of our laboratory staff according to the method outlined. These results are presented in Fig. 1. This group consisted of seven normal women and four normal men. The average increase in urine volume in the 90-, 120-, and 150-minute urine collections were 261, 272, and 260 per cent. These were calculated on the basis of the 60-minute urine specimen as previously described. In the test, the 90- and 120-minute outputs are critical from the standpoint of determining the antidiuretic effect, for it is during either or both of these periods that the antidiuretic effect is manifested. During these periods in this control group, the maximum increase in urine volume was 590 per cent, and the minimum in-

crease was 89 per cent for any one individual. The decrease in the chloride concentration which is typical of the electrolyte change resulting from water diuresis averaged 52, 64, and 89 per cent of normal for the three consecutive periods. The maximum chloride concentration during the critical period for any individual was 228 per cent, and the minimum concentration was 9 per cent.

This was contrasted with the controls who were given Pitressin without any steps taken to inactivate it (Fig. 1). The average urine volume for each of the three consecutive periods was 60, 32, and 94 per cent below the base line. Similarly, the average increase in chloride concentration for the three consecutive periods was 200, 431, and 136 per cent, with individual variations in chloride concentration in the critical group from 1,240 to 228 per cent.

II. Inactivating Ability of the Whole Blood of Normal Pregnant Individuals During the Last Half of Pregnancy.—Citrated whole blood was obtained from 24 normal pregnant patients whose gestation was of twenty or more weeks' duration, and was incubated with Pitressin as previously described. These results are given in Fig. 1. The average consecutive urine volumes for this group were 173, 172, and 152 per cent of the base-line values. The individual range during the critical period was 400 and 53 per cent. The average chloride concentrations during the three periods were 60, 70, and 83 per cent of the base line with individual variation during the critical period of from 10 to 108 per cent.

III. Inactivating Ability of the Whole Blood of Toxemia Patients During the Last Half of Pregnancy.—Citrated whole blood was obtained from 13 patients who were hospitalized at twenty or more weeks' gestation because of toxemia. The blood of these individuals was incubated with Pitressin and similarly evaluated. Fig. 1 illustrates these results. In this group, the average urine volume for the three consecutive periods was 182, 172, and 101 per cent of the base line. An individual variation of from 560 to 52 per cent occurred during the critical period. The chloride concentration averaged 67, 68, and 131 per cent for each of the three periods with an individual variation of from 125 to 16 per cent during the critical period.

IV. Inactivating Ability of the Whole Blood of Normal Pregnant Patients During the First Half of Pregnancy.—Nineteen individuals whose gestations were of less than twenty weeks' duration were investigated as to the ability of their citrated whole blood to inactivate the antidiuretic effect of Pitressin. The duration of their gestations ranged from eight to nineteen weeks, inclusive, and the results are summarized in Fig. 2. The eight to ten weeks, inclusive, group evidenced no inactivation. The individuals comprising the eleven to seventeen weeks, inclusive, group were variable in their ability to inactivate the antidiuretic effect of Pitressin. For example, inactivation occurred in one out of two individuals in the eleven weeks group; in one out of two individuals in the fourteen weeks group; and was present in one, and borderline in two of the three individuals comprising the seventeen weeks group. From eighteen weeks on, inactivation was present in all instances.

V. Additional Observations.—In order to determine which portion of the citrated blood of pregnant individuals was responsible for this inactivation, citrated blood was obtained from individuals in the third trimester of pregnancy. The citrate solution alone produced no inactivation when incubated with Pitressin. Serum produced a minimal or else a borderline inactivation. Pregnant individuals were then cross-matched with normal males. Citrated whole blood was obtained from each and the plasma was separated from the cells. The cells from each group were washed three times with saline. Then the plasma from the pregnant group was added to the cells from the male group and plasma from the male group was added to the cells from the pregnant

group. Pitressin was then added, and incubation and evaluation were made in the routine manner. It was found that plasma from the pregnant group when combined with male cells produced inactivation, but that male plasma combined with cells from the pregnant group failed to inactivate the antidiuretic effect of Pitressin. Male plasma and male cells when incubated with Pitressin produced no inactivation. It was noted that if the pregnant cells were not washed, they would produce inactivation of the Pitressin antidiuretic effect, and that the saline washings from these cells would likewise produce inactivation. Hence, it was concluded that the factor or factors responsible for this inactivation were contained in the blood plasma of pregnant women and that the potency of this was such that the small amounts which remained with the unwashed cells or was contained in the washings from these cells would inactivate the antidiuretic effect of the amount of Pitressin which we employed.
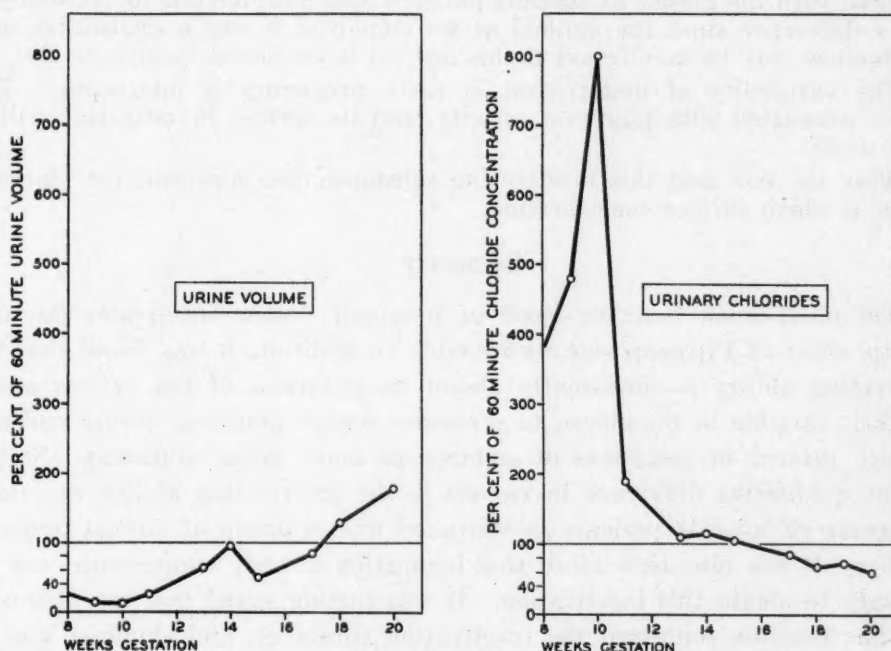

Fig. 2.—Inactivation of Pitressin antidiuretic effect during early pregnancy (mean values).

It was of interest to determine the importance of incubation in this inactivating process, and it was found that inactivation would occur if the mixture of Pitressin and whole blood was allowed to stand for one hour at room temperature, or if it was placed in an ice bath for a corresponding period of time.

It was of interest to determine if this inactivating substance crossed the placental barrier. To date, three patients have been studied in this respect. These individuals were delivered by cesarean section. Prior to clamping the umbilical cords, fetal blood was obtained from each and this fetal blood showed no inactivation as contrasted with the maternal blood of these individuals which showed the inactivation phenomena.

Comment

It may be said that the method of Dieckmann and associates which was employed in this study was a simple and effective means for the evaluation of Pitressin antidiuretic effect.

We have not as yet investigated this inactivation which has been described other than to determine that it is primarily a function of the plasma of pregnant individuals. Heller and Urban[9] have suggested the dual process of adsorption and enzymatic destruction as the means of this inactivation. Werle's[21, 22] work with the inactivation of the oxytocic and vasopressor effects suggests that this inactivation process may be the result of a specific enzyme. The fact that we have found that this inactivation will take place at room or ice bath temperature does not preclude enzymatic destruction. The observation that the combination of male plasma and the cells of pregnant individuals produced no inactivation would indicate that adsorption by these cells is a minor if not a nonexistent factor in this inactivation process, although adsorption by constituents of the plasma is not eliminated. The fact that we could detect no significant difference in the inactivating effect of the plasma of normal pregnant patients as compared with the plasma of toxemia patients does not preclude the existence of such a difference since the method as we employed it was a qualitative one. A difference may be manifested if this method is employed quantitatively.

The variability of inactivation in early pregnancy is interesting. This may be associated with placental activity, and its further investigation will be worth while.

Also, the fact that this inactivating substance does not cross the placental barrier is worth further consideration.

Summary

The observation that the blood of pregnant women inactivates the antidiuretic effect of Pitressin was confirmed.[5] In addition, it was found that this inactivating ability is consistently absent in gestations of ten or less weeks' duration, variable in the eleven to seventeen weeks' gestation group, and consistently present in gestations of eighteen or more weeks' duration. No significant qualitative difference in respect to the inactivating ability was noted in a group of toxemia patients as compared with a group of normal pregnant patients. It was also ascertained that incubation at body temperature was not necessary to obtain this inactivation. It was further noted that the plasma of pregnant patients contained the inactivating substance, and evidence was obtained to indicate that this inactivating substance does not cross the placental barrier.

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THE COMBINED USE OF INTRAVENOUS ETHYL ALCOHOL AND INTRAVENOUS PITOCIN

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THE use of ethyl alcohol for analgesia and anesthesia, according to Keys,[1] dates back to 1513 when alcohol fumes were first used for anesthesia. In 1920 Behan[2] used intravenous alcohol for the treatment of postoperative pain. In 1929 M. G. Marin[3] of Mexico City stimulated great interest in the use of alcohol in surgical anesthesia in his thesis, "Intravenous Anaesthesia with Ethyl Alcohol." This paper was followed by many reports in the literature concerning the use of intravenous alcohol for anesthesia, most of which were derogatory because of the narrow margin between the anesthetic and the lethal dose of alcohol.

More recently many reports have appeared by Rice,[4] Reimann,[5] Moore,[6] Mueller,[7] and Caffey[8] on the use of intravenous ethyl alcohol in the postoperative care of a patient. The latest report by Karp and Sokal[9] states that they have used intravenous alcohol successfully with more than two thousand patients. The advantage, as pointed out by these many authors, is the safe manner in which they are able to produce a sedative, analgesic, hypnotic, euphoric, vasodilatory, caloric, and antipyretic effect in the routine postoperative patient.

In 1950 Belinkoff and Hall[10] were the first to report the use of intravenous alcohol to produce analgesia during labor. In 1951 Chapman[11] confirmed their findings. Fetchko and associates[12] reported its use for preinduction analgesia before starting inhalation anesthesia for delivery.

The purpose of this paper is to report the use of intravenous alcohol for analgesia during labor in combination with intravenous Pitocin induction of labor. It was routine at this hospital to induce labor in all patients at term, when the cervix was one finger dilated and the presenting part was engaged. The only contraindications were grand multiparity, toxemias, cases of excessive vaginal bleeding, and cephalopelvic disproportion. It, therefore, seemed logical to combine ethyl alcohol with the intravenous Pitocin during the induction of labor in order to obtain an additional safe analgesic agent.

Procedure

The solutions were given into an antecubital or forearm vein through a 19-gauge needle. The needle was connected to two bottles by means of a Y tube, thus making it possible to control the rate of flow of each bottle separately. One of the bottles contained a solution of one oxytoxic unit of Pitocin to 50 c.c. of 5 per cent dextrose in water and the other a solution of 7½ per cent ethyl alchol in 5 per cent dextrose in water. The patient was not informed what the solutions were. After the Pitocin was started, she was asked to indicate the onset of her pains, and at that time the intravenous alcohol was begun. The rate of flow of the alcohol was rapid until the effect was noted by the patient and then the rates of flow of both solutions were governed by the clinical response

of the patient. The Pitocin was stopped when the cervix was fully dilated, but the alcohol was continued until the spinal anesthesia was given. Additional medication in the form of Demerol and scopolamine was given if the patient requested it.

Results

The results shown in Table I are the averages of the first 30 cases. No barbituates were given after the first 2 cases, since they were found to be unnecessary. The dosages of Demerol and scopolamine were decreased to one-third to one-fourth of what were used at this hospital prior to the usage of intravenous alcohol. The clinical sedative response to Demerol was found to be greatly increased when an adequate amount of alcohol had been given. The intravenous alcohol apparently had no effect on the induction of labor by the intravenous Pitocin and no contraindication to their combined usage was found. With one exception, all the patients were well pleased with the analgesia during the labor. The amnesia produced was still found to be proportionate to the amount of scopolamine given. The one dissatisfied patient wanted complete amnesia, but considered her labor pains no more severe than those she normally experienced with her menstrual periods. All the multiparous patients considered it the easiest labor that they had had. The infants delivered after this form of combined induction and analgesia cried spontaneously and showed no evidence of respiratory depression.

TABLE I

DURATION LABOR (HOURS)		ALCOHOL 7½% (C.C.)	PITOCIN 1:50 (C.C.)	DEMEROL (MG.)	SCOPOLA- MINE (MG.)	SECONAL (MG.)
PRIMIPARAS	MULTIPARAS					
7.3	4.8	744	413	125	0.52	18.1

Comment

The author does not wish to imply that a panacea for the combined induction and sedation of labor has been found, but presents these cases as testimony for an addition to the armamentarium of the obstetrician. The combined use of Pitocin and alcohol showed no antagonistic effects but, on the contrary, they seemed to have a synergistic effect. The alcohol did not slow the reaction of the Pitocin; it gave good, safe analgesia for the patient, and, at the same time, there was no respiratory depression in the babies.

There were no contraindications found to the combined use of intravenous ethyl alcohol and intravenous Pitocin.

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THE CONSERVATIVE TREATMENT OF ECLAMPSIA

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DESPITE the numerous prophylactic measures that have markedly reduced the incidence of toxemia of pregnancy, eclampsia still exists. The etiology is a supposition and explanations must be labeled as theories. This fact alone prevents a direct scientific attack. Certain empiric treatments that have evolved both by scientific methods and by trial and error are known to alleviate this condition. The combinations of science and art used in treating eclampsia are voluminous. This paper will show our method and give the results obtained at the Medical College of Alabama. The report covers six years on the charity service at the Jefferson Hillman Hospital beginning on July 1, 1945, and ending June 30, 1951.

Material

We have had 12,920 clinic deliveries during this six-year period and have had 74 cases of eclampsia, giving an incidence of 1 in 174.6. During this same period we have diagnosed 1,179 cases of pre-eclampsia. Table I shows the reported incidence of eclampsia.

TABLE I. INCIDENCE

LOCATION	INCIDENCE
Algiers, Africa[1]	2.85%
Charlotte, N. C.[1]	7.2%
Mean Index for world[1]	1.0%
Mean Index for U. S. A.[1]	0.66%
Univ. of Amsterdam Womans Clinic (1938-1948)[2]	0.6%
Maternity Hosp., Univ. of Cleveland (15 years, 1951)[3]	0.21%
John Gaston Hosp., Memphis (1938-1940)[4]	1.38%
John Gaston Hosp., Memphis (1942-1944)[4]	1.07%
Jefferson Hosp., Philadelphia (Bernstine) (1927-1945)[5]	0.43%
Charity Hosp. (L. S. U.) (5 years, 1945)[6]	1.07%
Margaret Hague Hosp. (1926-1932)[7]	0.92%
Jefferson-Hillman Hosp. (Present series) 1951	0.5%

A study of our 74 eclamptic patients shows several interesting facts. Sixty-five patients were Negro and nine were white. Of the 12,920 patients delivered at the Jefferson Hillman 9,763 (75.5 per cent) were Negro and 3,156 (24.5 per cent) were white. This gives an incidence of 0.28 per cent among white and 0.65 per cent among Negro. Fifty-eight and one-tenth per cent (58.1 per cent) of the patients had convulsions during the antepartum period, while 10.8 per cent were intrapartum, and 31.0 per cent were postpartum. Forty-nine of the convulsive cases occurred in primigravidas (66.2 per cent), twelve occurred in secundigravidas (17.6 per cent), and 16.2 per cent in gravidas iii or more (three cases in gravidas xi). Of the 74 patients, 32 attended the Jefferson Hillman Clinic. If the patient was seen only once in the clinic she was considered as having had prenatal care. Many of these patients did not attend

the clinic regularly and many did not follow the advised treatment. Fifteen attended the Public Health Clinics where the antepartum care was offered. Five were given antepartum care by private physicians (these cases were referred to the hospital after convulsions began). Twenty-three had no antepartum care whatsoever. It can be said fairly that most of the patients with eclampsia were given inadequate antepartum therapy for one reason or another.

In this series we had two maternal deaths, which represents a gross maternal mortality of 2.70 per cent. One of these patients died of a cerebrovascular accident shortly after admission and the second of infection on the ninth postpartum day.

CASE 1.—M. W., A15880, a 40-year-old Negro woman, para vii, gravida viii, obtained prenatal care at a public health clinic but did not return for two months prior to admission to the hospital. She was admitted on Aug. 16, 1949, at 11:00 A.M. with a history of headaches, ankle edema, and three convulsions two hours before admission. The patient was irrational on admission. The blood pressure was 250/170 and the pulse 120. The lungs were clear. The abdomen showed an eight months gravid uterus with the fetal heart tones in good condition but no contractions present. There was no peripheral edema.

Sedation and hypertonic fluids with magnesium sulfate added were given. The first temperature recorded was 106° F. Shortly after admission the patient had a generalized convulsion. The respiration became labored and bubbling in type. Six hours after admission she became completely comatose and grew progressively worse, death occurring 22 hours after admission, while she was still undelivered. The output totalled only 500 c.c. Impression as to cause of death was cerebral embolus and pulmonary edema. Autopsy permission was not granted.

CASE 2.—L. P., 27473, a 32-year-old Negro woman, para ii, gravida iii, was admitted on Aug. 6, 1946, with a history of ankle edema, headaches, and weight gain of three weeks' duration. Treatment by a private physician consisted of oral magnesium sulfate. Two hours prior to admission the patient had two generalized convulsions. There was no history of labor pains. The blood pressure was 230/130 and the fundus was the size of an eight months' pregnancy and not contracting. The fetal heart tones were not heard. There was two plus pitting edema of the legs.

Treatment consisted of sedation, hypertonic fluids with magnesium sulfate added, and nasal oxygen. Her condition did not improve. The membranes ruptured one day after admission. A live premature infant was delivered spontaneously in bed after a labor of three hours. The patient improved for two days and the urinary output increased; however, a gradually rising temperature occurred for which no cause could be found. The patient died on the ninth postpartum day with a temperature of 106° F. Autopsy permission was not obtained.

The treatment of eclampsia is directed primarily toward the mother, but fetal salvage is of no small concern. We have had nine fetal deaths which represent a gross fetal mortality of 12.1 per cent. One infant died in utero with the mother, three were premature, and five were term babies.

Table II shows maternal and fetal mortalities in cases of eclampsia from several large medical centers.

There are numerous methods of treating eclampsia that yield satisfactory results. This fact indicates that there are several methods by which the eclamptogenic process can be blocked or reversed. Therefore, the effects of these treatments should show up the principles involved. They are these:

1. Stop convulsions and prevent their future development.
2. Promote diuresis.
3. Reduce the blood pressure.
4. Maintain tissue fluid equilibrium.
5. Maintain conservative attitude toward delivery.

In the patient with convulsions whether ante partum, intra partum, or post partum, the treatment is essentially the same. To stop convulsions we use predominantly barbiturate sedation. Sodium Amytal is given slowly intravenously until convulsions cease and until the patient is asleep. Usually 0.5 Gm. is adequate. Respirations are carefully observed during this period. We have seen a decrease in the respiratory rate but have not witnessed apnea while administering the drug. We find barbiturates the most effective group of drugs because they are general nervous system depressing agents. They are unlike morphine sulfate in that they depress the brain and the cord whereas morphine depresses the brain but stimulates the cord. In addition to the sedation difference, barbiturates do not tend to have the antidiuretic effect that morphine exhibits.[14] For these two reasons we have used less and less morphine, the exception being the case of frank or impending cardiac failure.

Following deep sedation we give slowly 20 c.c. of 10 per cent magnesium sulfate intravenously. Cardiac behavior is carefully observed during this administration for evidence of standstill. An abnormal cardiac rhythm has not occurred from this medication, nevertheless, we always have calcium chloride available for immediate use. Magnesium is used to stop and prevent convulsions because peripherally it has a curarelike action and centrally it produces a true depression.[15] We do not use more than 8 Gm. of magnesium sulfate parenterally during a twenty-four hour period for fear of toxicity. Hypertonic glucose, namely 500 to 1,000 c.c. of 20 per cent in distilled water, is administered intravenously. It is used to produce diuresis with subsequent reduction in tissue edema. This elimination procedure is begun early in the regimen because clinical improvement accompanies diuresis. A medication that would prevent this process is contrary to our principles of therapy. Veratrum viride[14] and continuous spinal anesthesia cause an initial, if not prolonged, depression of urinary output due to the drop in blood pressure which they produce.

Augmentive drugs are used as needed. Oxygen is administered by nasal catheter or by tent if the patient has slow respiratory excursions, labored respirations, or is cyanotic. This is continued as long as is clinically indicated. Prophylactic penicillin is started in most cases. Digitalis is rarely used during the first 24 hours of treatment despite the presence of tachycardia, pulmonary and dependent edema. A patient with the previously forementioned findings and, in addition, a slowed circulation time and/or cardiac irregularity may be given quick-acting digitalis.

TABLE II. MATERNAL AND FETAL MORTALITY

AUTHOR	YEAR	YEARS' COVERAGE	CASES	MATERNAL MORTALITY	FETAL MORTALITY
Garber, Cincinnati[8]	1950	19	196	1.5%	
Whitacre, Memphis[4]	1940	8	70	21.4%	
Whitacre, Memphis[4]	1944	2	70	14.3%	20%
Bryant and Fleming, Cincinnati[9]	1940		120	1.67%	28.8%
Schwarz and Dorsett[10]	1930		186	7.0%	
Bernstine and Price, Philadelphia[5]	1945	18	62	16.1%	37.7%
Rhodes and Schmidt, Cleveland[3]	1945	15	121	12.9%	
Rhodes and Schmidt, Cleveland[3]	1950	5	34	2.9%	
Irving, Boston[11]	1937	15		27.4%	
Irving, Boston[11]	1946	6	32	6.3%	45.5%
Binder, Margaret Hague, clinic patients[7]	1932	6	52	5.8%	
Binder, Margaret Hague, nonclinic patients[7]	1932	6	71	15.3%	
Torpin, Augusta[12]	1940	20	350	12.8%	33%
Arnell, New Orleans[6]	1945	5	142	0%	24.2%
Bazan and Imoz, Buenos Aires[13]	1946	25	138	5.52%	12.33%
Jefferson Hillman (Present Series)	1951	6	74	2.7%	12.1%

During the course of the disease immediately following convulsions we continue the drugs mentioned previously. The sedation is then given subcutaneously as sodium phenobarbital 0.032 to 0.065 Gm. every one to four hours as needed to keep the patient absolutely at rest. One thousand c.c. of 20 per cent glucose in distilled water with 20 c.c. 10 per cent magnesium sulfate added is given every eight hours. If pulmonary edema is present, the fluid is given as 500 c.c. of 20 per cent glucose or as 50 c.c. of 50 per cent every three to four hours. Magnesium sulfate is given with each ampule of glucose if this does not exceed 8 Gm. in 24 hours. Augmentive drugs are continued or added as necessary.

We do not hesitate to use large amounts of barbiturate. The amount needed to get the desired clinical response is the proper dose. Despite possible liver damage we have not seen any toxic manifestations even after prolonged administration of these sedatives. We have used paraldehyde after the first day but have abandoned it because of the pulmonary edema it apparently produces. Despite frequent turning of the patient and oxygen administration, pneumonitis frequently develops during the use of paraldehyde. This is decidedly obviated with barbiturates. Occasionally paraldehyde is used if inadequate sedation with barbiturate occurs. When used it is not continued longer than absolutely needed.

The eclamptic patient is placed in our eclamptic room where side rails are used on the beds. During the first stage of treatment we do not examine the patient extensively for fear of precipitating more convulsions. The blood pressure, pulse, and respirations are checked each hour. Padded tongue blades are used to keep the patient from chewing the tongue during a convulsive episode. The lungs are auscultated frequently and the patient is turned regularly. A retention catheter is placed in the bladder and urinary output is carefully measured. The urine is checked for albumin and red blood cells daily. A routine blood count, urea nitrogen, uric acid, and if indicated carbon dioxide combining power determinations are obtained soon after the case is diagnosed. Laboratory tests are repeated as indicated by the patient's condition. After the first 24 hours an ophthalmoscopic study is made and neurological examination, circulation time, and any other special studies are done as indicated.

After the first 24 hours, unless there is evidence of muscular irritability, we begin to decrease the sedation and to allow the patient to arouse for short intervals between doses. During the semilucid intervals, nourishment and water are administered by mouth. A liquid sodium-poor diet, which is high in proteins, is given. Skimmed milk powders mixed in skimmed milk with eggs added are frequently used. If the patient is not excessively obese we add sugar to this mixture.

Day by day the sedation is decreased until the patient is taking phenobarbital, 0.05 Gm. four times a day by mouth. This dosage is usually continued until after delivery or until further treatment is unnecessary. Magnesium sulfate by mouth is given each morning to the edematous patient as soon as she can call for a bed pan. The hypertonic fluids and purgation are discontinued as soon as the edema is gone. Edema due to hypoproteinemia must be kept in mind in this treatment. Parenteral magnesium sulfate is discontinued as soon as the blood pressure has dropped to subcritical levels. Diet is increased daily in proteins and carbohydrates. Vitamins, iron, and calcium are added as necessary.

If the patient has true eclamptogenic toxemia without hypertensive vascular disease or hypertensive cardiovascular disease, she shows a rather dramatic response to this treatment. The blood pressure drops to a much less critical level (150-160 systolic) or even on occasions to normal levels. The tissue fluid is shifted and diuresis begins.

There are recalcitrant cases that require perseverance in the treatment but they too respond under the art of proportioning the drugs of this regimen.

The postpartum patient with eclampsia is treated as outlined above. The intrapartum case is treated in the same manner with the possible exception of less sedation.

Most of our undelivered patients go into labor before the first 72 hours have elapsed. We keep the laboring patient sedated with barbiturates and seldom need Demerol or scopolamine. We use 1 per cent procaine pudendal block anesthesia for the delivery. If the patient is at term and does not deliver during the first 72 hours we induce labor by stripping the membranes, rupturing the membranes if the head is engaged, or by using a bougie in the cervix. Pitocin is not used primarily because of its vasopressor action. If the patient is not at term we make every attempt to maintain the pregnancy until the thirty-sixth week. Of course, if the patient's condition fails to show improvement, interruption of the pregnancy is indicated by the means most suitable to the individual case. We have not found cesarean section necessary in any of these 74 cases. A conservative attitude yields gratifying results. The results obtained on our service, both fetal and maternal, clearly indicate that abdominal delivery should be reserved for the patient with true obstetrical indications.

Once the patient has overcome the disease she should be studied, particularly as to cardiac and renal functions, in order that prognostic and future therapeutic advice might be given intelligently.

Summary and Conclusions

1. The results of treatment of seventy-four cases of eclampsia at the Jefferson-Hillman Hospital from July 1, 1945, to June 30, 1951, are presented.

2. Nothing new has been added to the general principles of therapy in this disease. One method, namely, sedation, hypertonic fluids, and magnesium sulfate, combined with close observation of the patient and conservative delivery, is used.

3. Cesarean section was not found necessary in any case.

4. The gross fetal mortality was 12.1 per cent while the maternal mortality was 2.70 per cent.

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EXTRAPERITONEAL CESAREAN SECTION. EXPERIENCE WITH THIRTY CASES

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CESAREAN section by experienced surgeons is, today, a relatively safe procedure. Pitfalls occur mainly in the presence of infection. This element and hemorrhage are the principal causes for maternal death following the operation.

The management of the cesarean case in which infection is actual or potential always has been a serious problem. A readily available solution is the extraperitoneal paravesical cesarean section as employed by the late Dr. Norton. The purpose of this paper is to review our experience with this procedure.

Material and Methods

During the two-year period from June, 1949, to June, 1951, 539 cesarean sections were performed at the Queen of Angels Hospital, Los Angeles. Extraperitoneal section was employed in 32 (5.9 per cent). The paravesical approach of Norton was used in 30 of these 32 cases and, in this institution, has replaced, to a large extent, the retrovesical approach of Waters.

Both the private and the ward services were represented in these 30 cases. The operations were performed by the authors, the teaching staff, and the resident staff. Twenty-two of the patients were primigravidas ranging in age from 16 to 35 years; 8 were multigravidas of 23 to 39 years of age.

Indications

The indications for delivery by the abdominal route in this series of 30 cases are given in Table I.

Cephalopelvic disproportion was present in 14 cases, in all of which there was adequate trial of labor. Of these, 4 were complicated further by pre-eclampsia, 2 by fetal distress, and one by antepartum death of the fetus.

There were 6 abnormal presentations: one frank breech, 2 brow, and 3 compound. The latter were (1) a prolapsed arm in association with a transverse presentation, (2) a prolapsed arm over the vertex with a nonnegotiable cervix, and (3) a prolapsed arm over a frank breech with intrapartum death of the fetus.

Uterine inertia was the indication for abdominal delivery in 5 cases, 2 of which were further complicated by pre-eclampsia.

Fetal distress during labor was the indication in 2 cases.

Pelvic deformity in 2 cases resulted in dystocia; in each the abnormality consisted in a sharp angulation of the sacrum with a marked curvature of the coccyx.

There was one case of repeat section with a history of ruptured membranes for 312 hours.

TABLE I. INDICATIONS FOR ABDOMINAL DELIVERY

Cephalopelvic disproportion after adequate test for labor		14
Cephalopelvic disproportion alone	7	
With irregular fetal heart tones	2	
With pre-eclampsia	4	
With dead fetus	1	
Abnormal presentation		6
Brow	2	
Prolapsed arm	3	
Breech	1	
Uterine inertia		5
Uterine inertia alone	3	
With pre-eclampsia	2	
Fetal distress		2
Pelvic deformity		2
Previous cesarean section		1
Total		30

The extraperitoneal route for abdominal delivery was selected in these 30 cases because of potential infection. The criteria are listed in Table II.

TABLE II. INDICATIONS FOR EXTRAPERITONEAL ROUTE

Labor of 24 hours or more		10
Membranes ruptured less than 12 hours	2	
More than 12 hours	8	
Membranes ruptured more than 12 hours with less than 24 hours' labor		9
Previous vaginal manipulations or attempted delivery from below exclusive of above		11
Total		30

TABLE III. COMPLICATIONS OF EXTRAPERITONEAL SECTIONS

COMPLICATION	NUMBER	PER CENT
Peritoneum opened	1	3.3
Bladder opened	1	3.3
Postoperative morbidity	6	20.0
Postoperative distention	0	—

Labor of more than 24 hours' duration had been in force in 10 patients, in 8 of whom the membranes had been ruptured more than 12 hours.

Rupture of the membranes for more than 12 hours, but with less than 24 hours' labor, was the indication in 9 patients.

In the other 11 cases there was a history of manipulations other than a few rectal examinations and/or one ideally guarded vaginal examination, or a history of failure of attempt to deliver through the vagina.

Complications

The immediate and postoperative complications are listed in Table III.

The peritoneal cavity was entered inadvertently during surgery in one case and the bladder in another.

The postoperative course in every patient was uneventful; neither ileus nor distention occurred.

The postoperative morbidity, based on the classification of the American College of Surgeons, was 20 per cent for the entire series. Six patients had a total of 14 days of morbidity or an average of 2.3 days each; in none was the morbidity of serious consequence. This rate compares favorably with that for all cesarean sections during this period. The over-all cesarean morbidity was 17 per cent with an average of 3 days of morbidity per case, while that for emergency sections was 26 per cent.

Results

Maternal deaths did not occur in this series. There were 2 fetal deaths, one before the onset of labor and the other during labor. Since both were known to have occurred before surgery, the fetal deaths cannot be attributed to the operative procedure.

Comment

Extraperitoneal cesarean section is reputed to have many disadvantages: that it is a difficult procedure to master; that it is fraught with danger to the bladder, the ureter, and the uterine vessels; that exposure for extraction of the infant is poor. Our experience with this procedure does not substantiate this bad reputation. We are convinced that facility in this operative procedure can be readily acquired by any trained obstetrician.

Hazards encountered during surgery in this series were minimal. There was only one instance of injury to the bladder (3.3 per cent), in spite of the fact that many of these operations actually were performed by the resident staff. The peritoneal cavity was entered but once (3.3 per cent), and the opening was closed by simply placing a suture around the aperture.

In regard to actual delivery, we have observed that exposure of the lower uterine segment can be enhanced by severing the lateral obliterated hypogastric artery. An S-shaped longitudinal incision in the uterus will increase further the ease of extraction of the infant. The largest infant delivered in the series was 10 pounds, 5 ounces. Forceps rarely were required. If the head of the infant is disengaged vaginally prior to the section, delivery at operation is facilitated.

The advantages of the paravesical extraperitoneal route are numerous. Peritonitis is avoided since intraperitoneal spillage of infected amniotic fluid cannot occur, nor will there be postoperative seepage through a peritoneal suture line from a nidus of infection in the uterus. Postoperative ileus is reduced to a minimum. Because the peritoneal cavity is not entered, postoperative adhesions should not form and the danger of evisceration is nonexistent.

The actual operating time is only slightly lengthened.

Obstetricians who have, in their armamentarium, facility in the use of extraperitoneal section may permit a longer trial of labor. Waters[2] states that he has been able to reduce his incidence of cesarean section by half since he has been employing this type of operation. We do not, however, advocate unnecessarily prolonged trials of labor and do not hesitate to use the procedure in potentially infected cases if fetal distress occurs. This complication, manifested by irregular fetal cardiac rate, is a real threat to the survival of the infant. During the two-year period covered by this report the incidence of fetal distress in 92 cases of cephalopelvic disproportion requiring cesarean section after a trial of labor was 16 per cent with a fetal mortality of 27 per cent.

In this study extraperitoneal cesarean section was performed twice with the knowledge that the fetus was dead. The first case was that of a multipara at term whose membranes had been ruptured for 48 hours, who had been in desultory labor for 10 hours and in whom the fetal heart could not be heard. A dead fetus weighing 6 pounds, 15 ounces was delivered by extraperitoneal cesarean section. The frank breech presentation was complicated by a prolapse of the right arm. The incidence of this complication is extremely low. It occurred four times in 42,410 viable deliveries at Johns Hopkins University Hospital as reported by Eastman.[3]

The second case involved a 40-year-old primigravida in whom the fetal heart could not be heard at term, at the time of a routine antepartum office

visit. Labor commenced three days later. After an adequate trial of labor, in the presence of a cephalopelvic disproportion, a 10 pound, 5 ounce dead fetus was delivered by extraperitoneal cesarean section.

Some obstetricians will question the wisdom of any type of abdominal delivery when the fetus is dead. Reports in the literature, however, corroborate our views in this regard. Briscoe[1] does not hesitate to perform an extraperitoneal cesarean section when the fetus is dead and when there is indication, rather than to resort to dangerous and traumatic vaginal deliveries that may lead to chronic invalidism. That difficult vaginal deliveries and such procedures as craniotomy have no place in modern obstetric practice is substantiated in the following statistics: The maternal mortality was 3.4 per cent in 81 vaginal embryotomies at the Margaret Hague Maternity Hospital as reported by Kurtz and his colleagues.[5] The maternal mortality was 7 per cent in 147 cases of craniotomy collected from the literature by Heffernan and Sullivan.[4] Twelve of 101 maternal deaths due to obstetric causes (11.8 per cent) at the Margaret Hague Maternity Hospital were due to hemorrhage or sepsis dependent on difficult vaginal delivery according to Cosgrove and Waters.[2]

Summary

Thirty cases of extraperitoneal cesarean section of the Norton type are reported. Potential infection coupled with necessity for abdominal delivery for obstetric complications was the indication in each instance. Injury to the bladder occurred in one patient (3.3 per cent), and the peritoneum was entered inadvertently in one other (3.3 per cent). Six patients experienced postoperative morbidity (20 per cent). Maternal mortality was zero and fetal mortality due to the operative procedure was zero.

Conclusion

The potentially or acutely infected parturient who must be delivered abdominally should be given the benefit of the best available surgical procedure, i.e., extraperitoneal cesarean section supplemented by chemotherapy and antibiotics.

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THE USE OF A SEMISYNTHETIC OXYTOCIC (METHERGINE)* IN THE THIRD STAGE OF LABOR

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IMPORTANT properties of an oxytocic are its ease of administration, its rapid onset of action and long duration, its lack of side effects, the absence of blood pressure changes, small blood loss, effective reduction of bloody lochia, etc. Methyl ergonovine tartrate (Methergine) is such an oxytocic as shown by the recent reports of Kirchhof,[1] Priver,[2] Bunch,[3] Williams,[4] Baskin,[5] Gipstein,[6] Riordan,[7] Gill,[8] and Schade.[9] This material, first prepared by Stoll and Hofmann,[10] is obtained by partial synthesis of lysergic acid and 2-aminobutanol. Because of a possible ergot shortage, we were prompted to evaluate for ourselves the effectiveness of this oxytocic. This report summarizes our results in a series of 157 deliveries.

Hemorrhage, next to infection, is the most common cause of maternal mortality. Hemorrhage during the third stage of labor is due to failure of the uterus to contract, so that any oxytocic that produces a rapid and prolonged effect on the uterus is a valuable aid in delivery. It must be remembered that an oxytocic must overcome also the relaxing effect of the analgesic employed.

A group of 157 patients (103 private and 54 ward) received Demerol (150 mg.) and scopolamine (1/200 grain) to relieve the pains of labor, and nitrous oxide and ether for delivery. Pitocin was used intramuscularly at the birth of the child and 1 c.c. of Methergine (0.2 mg. of d-lysergic acid dl-hydroxybutylamide-2) intravenously as soon as the placenta was separated. In this series, the placenta was palpated in the cervical opening. The action of the oxytocic was rapid. As soon as the contraction was palpated, a simple expression was practiced and the placenta was expelled almost immediately.

While accurate measuring of immediate blood loss is difficult, in this series it was estimated as 228 c.c. in the private cases and 228 in the ward patients. The lochia following delivery is a variable factor. In multiparas, there is frequently profuse lochia requiring the use of some oxytocic during the first two or three days post partum. During the puerperium, Methergine was given, one tablet twice a day for the first two days. In this series of cases, the lochia was reduced, and the uteri involuted satisfactorily. It also might be stated that episiotomies were done almost routinely. Blood pressure readings were done in all cases every 15 minutes for 3 hours post partum by resident physicians. The average hospital stay of these patients was six days. There were no patients in this series readmitted to the hospital for excessive postpartum bleeding. In all these cases, Methergine was not given until the placenta was completely separated from the wall of the uterus.

Results

Our cases can be divided into two groups, 103 private cases and 54 ward cases. Tables I and II summarize the results in the two groups, respectively.

TABLE I. PRIVATE CASES

Number of Cases.—		*Afterpains.—*	
Episiotomy	83	*Occurrence:*	
No episiotomy	20	Irregular	30
		After tabs	1
		Constant	18
Type of Delivery.—		None	54
Natural	91	*Severity:*	
Forceps	10	Light	20
Cesarean	1	Severe	19
Breech	1	Moderate	10
		None	54
Parity.—		*Nausea.—*	
Para i	29	*Occurrence:*	
ii	47	Irregular	30
iii	13	After tabs	5
iv	9	Constant	6
vi	2	None	62
x	1	*Severity:*	
2 not recorded		Light	18
		Moderate	16
		Severe	7
Age (Years).—		None	62
17-20	15		
21-25	41	*Headache.—*	
26-30	24	*Occurrence:*	
31-37	23	Irregular	25
Time Between Birth of Child and		After tabs	3
Expulsion of Placenta.—		Constant	6
Average of 103 cases	3.3 minutes	None	69
		Severity:	
		Light	10
Blood Pressure (Consecutive).—		Moderate	14
Constant	86	Severe	10
Slight drop	9	None	69
Slight rise	8	*Blood Loss.—*	
Mild hypertension but no harmful		50 c.c.	2
effects from Methergine		75 c.c.	3
10 of 103 patients		85 c.c.	1
		100 c.c.	7
		125 c.c.	6
		150 c.c.	19
Lochia.—		160 c.c.	1
Amount:		200 c.c.	24
Light	16	225 c.c.	6
Moderate	40	250 c.c.	14
Profuse	3	275 c.c.	2
Moderate then light	29	300 c.c.	1
Profuse then moderate	15	325 c.c.	2
Type:		350 c.c.	4
		400 c.c.	4
Alba	9	425 c.c.	1
Rubra then serosa	88	450 c.c.	3
Rubra	4	500 c.c.	3
Serosa then alba	2	Average about 228 c.c.	

Seven patients required uterine and vaginal packing.

One patient had premature labor at 36 weeks' gestation, a 4-pound baby.

Three patients were obese, 40 pounds overweight, one with a special diet during pregnancy.

One patient had an emergency appendectomy in her eighth month and results could not be included.

It can be seen that blood losses were low; that blood pressure changes were negligible; that lochia was reduced, and that placental expulsion followed rapidly after the birth of the child. The apparent differences in the incidence

TABLE II. WARD PATIENTS

Number of Cases.—		Afterpains.—	
Episiotomy	31	*Occurrence:*	
No episiotomy	23	Irregular	12
		After tabs	12
Type of Delivery.—		Contstant	28
Natural	44	None	2
Forceps	3	*Severity:*	
Breech	3	Light	7
Set of twins	1	Moderate	17
Manual removal of the placenta	1	Severe	2
Cesarean	2	None	28
		Nausea.—	
Parity.—		*Occurrence:*	
Para i	20	Irregular	4
ii	14	After tabs	1
iii	7	Continuous	2
iv	7	None	47
vi	4	*Severity:*	
vii	1	Light	2
viii	1	Moderate	5
		Severe	0
Age (Years).—		None	47
13-20	14	*Headache.—*	
21-25	20	*Occurrence:*	
26-30	10	Irregular	4
31-42	10	After tabs	1
		Continuous	1
Time Between Birth of Child and		None	48
Expulsion of Placenta.—		*Severity:*	
Average 54 cases	2.7 min.	Light	3
		Moderate	2
Blood Pressure (Routine).—		Severe	1
No change	49	None	48
Slight rise	2		
Slight drop	3	*Blood Loss.—*	
Patients with mild essential hyper-		None	4
tension but no harmful effects		50 c.c.	1
from Methergine	4 of the 54	60 c.c.	2
		75 c.c.	3
Lochia.—		100 c.c.	6
Amount:		115 c.c.	1
Light	3	150 c.c.	6
Moderate	43	200 c.c.	6
Moderate then light	7	250 c.c.	4
Profuse then moderate	1	300 c.c.	8
Type:		400 c.c.	3
Alba	3	535 c.c.	1
Rubra	33	600 c.c.	4
Rubra then serosa	18	750 c.c.	1
		Average, 228 c.c.	

Two required packing.

One bled at home but did not need hospitalization.

Four, not recorded.

and severity of afterpains, nausea, and headaches may be traced to the fact that the ward patient is less prone to psychosomatic symptoms and complaints.

Summary and Conclusions

It can be concluded from this study that Methergine is an efficient and rapidly acting oxytocic. It produces a prolonged contractile effect on the uterine musculature of the postpartum uterus. Blood loss was minimized, no

blood pressure effect was observed, and except for the complaint of afterpains, no untoward effects were observed. Oral Methergine was employed to hasten involution.

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437 WESTERN AVENUE

THIOUREA DERIVATIVES AND THE FETUS*

A Review and Report of a Case

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THE effects upon the fetus of thiourea derivatives given during pregnancy are not yet completely known. Thiourea derivatives can be most useful, since effective medical management of hyperthyroidism during pregnancy may allow successful completion of pregnancy and delay definitive therapy until a more fortuitous state of endocrine balance is reached.

The number of cases where the fetal effects of maternal treatment are recorded in the literature is small, totaling thirty. This is surprising, since thiourea derivatives have been easily available for almost six years, and the incidence of hyperthyroidism during pregnancy is somewhere between 0.06 and 0.3 per cent.[1, 2, 3] Certainly the infants born of mothers managed by potent antithyroid drugs should be of great interest.

Of the 30 reported pregnant women with hyperthyroidism treated with thiouracil or one of its derivatives, 25 had normal children, two with transient goiters. There was one spontaneous abortion, one therapeutic abortion, one anencephalic monster, one cretin, and one mother died suddenly in the sixth month of pregnancy (Table I).

Freiesleben and Kjerulf-Jensen[4] studied methylthiouracil in rats. They proved transplacental transmission of the drug by feeding the fetuses of methylthiouracil-fed mothers to other rats, which subsequently developed goiter. However, no change was found in the thyroids of the fetuses of the rats fed methylthiouracil. This last observation is not surprising when it is realized that colloid formation in the thyroid of the rat is little developed until the last of pregnancy (sixteenth day)[4, 5] and does not approach normal adult rat appearance until about the twenty-first fetal day.[6] However, Goldsmith and associates[7] found goiters in the young of rats fed thiouracil during pregnancy. The young soon became normal if fed no more thiouracil. That the drug is passed through the milk was also proved by the development of goiter in newborn rats after seven days of suckling from a mother fed the drug.[6] Williams[19] demonstrated that lactating women given thiouracil secrete the drug in high concentration in their milk. Even cretinism is produced in young rats by prolonged administration of methylthiouracil in the food after birth.[4] Hughes[8] produced myxedema, retarded bone development, anemia, retarded growth, and goiter in baby rats fed thiouracil after birth.

Schultze and Turner[9] demonstrated that the thyroid of the goat fetus is *not* influenced by thiouracil before mid-pregnancy but *is* influenced after this time. It is after mid-pregnancy that the goat thyroid normally begins to have

follicles. Chapman and co-workers,[10] by a series of radioactive iodine studies done in pregnancies terminated by therapeutic abortions, have proved that the human fetal thyroid begins to metabolize iodine after the twelfth week of gestation. Radioactive iodine given the mother was not stored in the thyroid gland of the fetus until the twelfth week of the pregnancy had passed. Anatomically and functionally the human thyroid approaches maturity by the fourth fetal month.[6]

TABLE I

AUTHOR	DURATION OF THERAPY	IODINE	RESULTS
Whitelaw[1]	1 month	0	Abortion, normal
	3 months	0	Anencephalic, normal
	5 months	0	Normal
Freiesleben[4]	3 months	0	Abortion, goiter
Vogt[11]	4 months		Normal
Strause[12]	2 months	+	Normal
Reveno[13]	4 months	0	Normal
	7 months	+	Normal
	9 months	+	Normal
McGavack[14]	4 months		Normal
Rose[15]	5 months		Normal
Palmer[16]	5 months	+	Normal
Eaton[17]	5 months	+	Normal
	9 months	0	Normal, transient goiter
Davis[18]	6 months	0	Maternal death, goiter
Williams[19]	9 months (3 cases)	+	3 Normal
	1½ months	0	Normal
	1 month	0	Normal
Sexton[20]	9 months (2 cases)	0	2 Normal
Astwood[21]	9 months (3 cases)	0	3 Normal
Hone[22]	7 months	0	Cretin, died
Wood[26]	9 months	0	Normal, transient goiter
Saslaw[27]	5 months	0	Normal
Acton[28]	3 months (1st trimester)	0	Normal
Eisenberg[29]	3 months		Normal

Summary of Table I.—Of 30 pregnancies complicated by hyperthyroidism treated with thiourea derivatives, 25 produced normal infants, two of whom had transient goiter. One cretin, whose goitrous gland may have been due to methylthiouracil, died shortly after birth. Two abortions, which were probably due to the primary maternal disease, occurred. One anencephalic monster, whose thyroid gland was normal, was produced. One mother and fetus died suddenly at the sixth month of gestation for an undiscovered reason. The fetus had a goiter. No goiters were found in infants whose mothers had received iodine in addition to a thiourea derivative.

Case Report*

The mother was a 34-year-old primigravida who had a history of six years of hyperthyroidism without obvious goiter. A subtotal thyroidectomy was done three and one-half years before pregnancy. The symptoms returned and her basal metabolic rate was brought to normal by propylthiouracil. A single attempt was made to discontinue the drug but a prompt relapse with weight loss, tremor, loose stools, and elevation of basal metabolic rate to plus 30 occurred. Propylthiouracil in 100 mg. daily doses controlled her symptoms until she became pregnant. During the first month of pregnancy it was necessary to increase the daily dose of propylthiouracil to 250 mg. which was maintained throughout the pregnancy. No iodine was given during her pregnancy. Her infant was born at term by an uncomplicated labor and delivery.

He weighed 3,495 grams (7 pounds, 12 ounces) at birth. A markedly enlarged, firm, symmetrical thyroid gland was present at birth. He was troubled for his first weeks of life with difficulty in swallowing which could be improved by hyperextending his head during feedings. On his fourth day of life the serum cholesterol was 82 mg. per cent

*Dr. Solomon J. Benensohn of Chicago very kindly referred this infant to us for study.

and by the ninth day this had risen to 128 mg. per cent. At age 2 months, the fasting serum cholesterol was 130 mg. per cent. Serial electrocardiograms on the second, eighth, and seventeenth days, and at 2 months revealed in the beginning low amplitude QRS complexes and low T waves with a pulse rate of 96 on the second day, 106 on the eighth day, 136 on the seventeenth day, and 140 at age 2 months. There was a steady shift toward a normal electrical pattern on the first three electrocardiograms and the last one was normal. X-rays of the bones on the second day of life revealed the presence of ossification centers of the distal femoral and proximal tibial epiphyses, and two tarsal centers were present. These are the usual findings for the mature newborn male. X-rays made at the second month revealed the appearance of 2 carpal centers, the center for the head of the humerus, and the third tarsal center. Thus, the rate of appearance of new centers was normal.
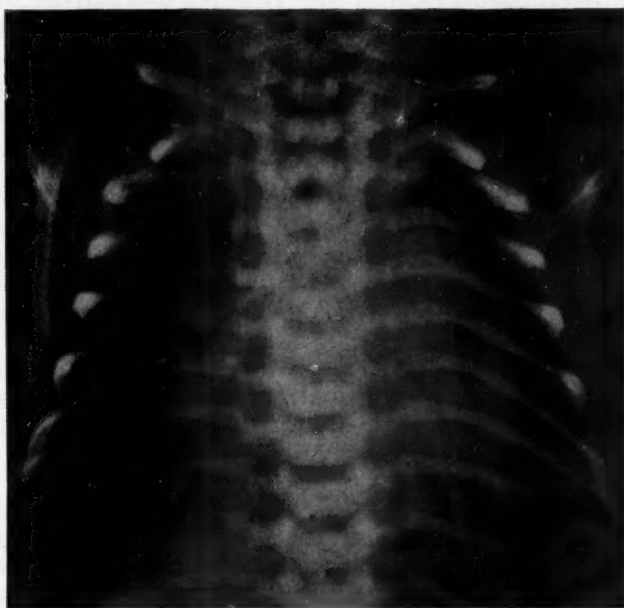
Fig. 1.—Chest x-ray at age 2 days. The cardiac shadow is large. The indentations in each lung apex are thought to be the lower poles of the thyroid gland.

His thyroid gland slowly decreased in size so that it was not visible at 18 days of age unless the head was allowed to fall into extreme hyperextension. At age 2 months small lateral lobes of the thyroid could still be seen when the head was held in extreme extension. The goiter finally disappeared by the age of 3 months. It is believed that the convex shadows at each lung apex in the x-rays made on the second day of life represent the lower poles of the thyroid gland (Fig. 1). These indentations were not present at age 2 months when the gland appeared externally much smaller.

He suffered neither constipation nor diarrhea during his first months of life, was active and alert, held up his head at one month and smiled. At five months he squealed at play, batted at and held toys in his hands, laughed, showed sociable tendencies, and sat with support. His cry was normal. He gained weight slowly at first but was in the normal range for height and weight by the age of 5 months. His growth and development thus revealed neither signs nor symptoms of either hypo- or hyperthyroidism.

Comment

The cretin born of a thyrotoxic mother treated with methylthiouracil[22] might seem at first thought the result of the therapy used. However, cretinism

does occasionally result from a pregnancy complicated by hyperthyroidism.[23, 24] Therefore, the abnormality may be related to the primary endocrine disturbance in the mother. This idea is further supported by the failure of thiourea derivatives to promote more than a transient enlargement of the thyroid gland in animals as well as in human beings[4, 7, 8] such as Eaton's case[17] and Wood's case.[26]

The anencephalic monster born to the hyperthyroid mother[1] treated with a thiourea derivative might also give rise to some concern about the administration of such drugs during pregnancy. However, to our knowledge, this case is the only one yet reported. Dean[24] in 1927 reported two successive anencephalic monsters born of a hyperthyroid mother who, of course, had received no thiourea drugs. There is no evidence to support the notion that anencephaly occurs more frequently in the offspring of thyrotoxic mothers than in offspring of normal mothers. There is no good evidence that thiourea derivatives may increase the incidence of anencephaly in the infants born to hyperthyroid women.

Electrocardiographic examination was immediately helpful in evaluating our patient's status. The low voltage pattern and slow pulse for the age along with the steady changes toward normal seen in repeated electrocardiograms were interpreted as signs of recovery following removal of an agent depressing the thyroid activity. By these examinations it may be possible to estimate the situation more rapidly than by repeated bone age determinations. Serum cholesterol measurement during the newborn period always gives a low figure which rises rapidly and could not be expected to be helpful at that time. Re-examination of the patient at age 2 months, and follow-up at age 5 months bore out the prognosis for normalcy made with the aid of the electrocardiograms during the newborn period.

The mechanism of thyroid enlargement in the patient presented is not well understood. Thiourea derivatives cross the placental barrier with ease.[4, 11] But, if the thyroid enlargement is due to the presence of these antithyroid drugs in the fetus it seems inconsistent that goiter does not occur more often in the newborn infants of mothers treated with thiourea derivatives.

Freiesleben and Kjerulf-Jensen[4] suggest that fetal disturbances may result from antithyroid drugs used in treatment of maternal hyperthyroidism. They believe that fetal goiter comes as a compensatory phenomenon in fetuses of women whose metabolism is depressed below normal by these drugs. Their experiments support this hypothesis, since giving thyroxin and methylthiouracil simultaneously to pregnant rats prevented the fetal goiter regularly seen when methylthiouracil was used alone. However, the lowest basal metabolic rate of the mother of the patient reported here was plus 15, and her total weight gain during pregnancy was less than twenty pounds. Drug-induced maternal hypothyroidism does not seem to be a factor in this case. Neither were Eaton's[17] or Wood's[26] patients thought to be hypothyroid.

Transplacental transmission of thyrotropic hormone seems unlikely, not only because of the lack of maternal goiter in the patient reported here, but because animal studies by Peterson[25] have failed to demonstrate transplacental passage of the hormone.

Since McGinty and Sharp[30] demonstrated in animals that iodine has an effect antagonistic to thyroid enlargement in animals treated with thiourea derivatives, this factor was investigated in the patients we have reviewed from the literature (Table I). No goitrous infants were born of mothers treated with a thiourea derivative plus some iodine during pregnancy. The only infants with enlarged thyroid glands were those whose mothers had received an antithyroid drug without iodine. These observations suggest two possibilities: one, that these antithyroid drugs interfere in some way with iodine transport to the fetus, and two, that iodine is necessary to inhibit the formation of thyrotropic hormone in the fetus. No evidence is available to support the first con-

tention except that partially thyroidectomized dogs produce goitrous pups unless the bitches are given iodine.[32]   Data on fetal blood iodine levels in pregnancies of patients treated with antithyroid drugs but not with iodine were not found by a search through the literature.   So far as the second contention is concerned, where some degree of maternal hyperthyroidism is allowed to persist, an excess of both iodine and thyroid hormone is available through the placenta of the fetus, and fetal thyrotropic activity may be inhibited.   But where the maternal thyroid activity is normal or depressed, the fetal thyrotropic response to transplacental antithyroid drugs may be maximal, and produce a large fetal thyroid gland.   This change in the thyroid gland may be of no importance, or produce mechanical difficulties with feeding or breathing, or be serious enough to produce severe neonatal hypothyroidism.

These observations suggest that when hyperthyroidism during pregnancy is treated with thiourea derivatives, iodine should be given the mother during the last month of the pregnancy to prevent goiter in the newborn infant.

Summary

1. A summary of some studies in animals and human beings on the fetal effects of thiourea derivatives in the literature is presented.

2. A survey of the literature found reports of 30 infants born of thyrotoxic mothers treated with thiourea derivatives during pregnancy.   Twenty-five infants were normal, two of whom had transient enlargement of the thyroid gland. One pregnancy produced a cretin; two pregnancies were aborted and one of these fetuses had a goiter; one mother died suddenly at the sixth month of pregnancy with an infant with a goiter; and one produced an anencephalic monster with a normal thyroid.

3. Among the thiourea derivative treated mothers, no goitrous infant was born of any mother who had received iodine during pregnancy, and all goitrous infants were born of mothers who had not received iodine during pregnancy.

4. A third normal infant with transient enlargement of the thyroid gland is reported.   His hyperthyroid mother was treated throughout her pregnancy with a thiourea derivative and received no iodine.

5. Iodine is recommended for the last month of pregnancy complicated by hyperthyroidism treated with thiourea derivatives.

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UPPER AGE LIMIT OF PARTURITION.

A Review of the Literature

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THE Bible says Sarah begat Isaac at the age of 90.[1] Today, courts of law must occasionally consider whether or not it is still possible for pregnancy to occur at an advanced age. In cases involving interests in property, legal precedent holds that a mature female is to be considered as able to have a baby at any age. Since it would seem likely that eventually law might wish to adjust to medicine in this matter, it is of interest to consider to what limit of chronological age female fertility has been reported.

The largest compilation of births by age of the mother is published in "U. S. Vital Statistics"; the most recent publication is for the year 1948.[2] There were approximately 3½ million births during this year, of which 168 were recorded as being in women 50 years or older. This incidence of about one in 20,000 births is borne out roughly by preceding yearly statistics published in this source. We believe it to be highly significant that the maternal age noted on the individual birth certificates is dependent upon the accuracy and veracity of the mother. It may be that there is even a greater ignorance of one's true age than the ratio of one in 20,000 would indicate. For example, it was noted that the percentage of Negroes over the age of 50 years giving birth is approximately and uniformly three times that of whites. The information from which these particular vital statistics are drawn make it questionable as to whether they should serve as legal evidence in judging the individual case.

Periodic reviews of their records by large American maternity hospitals may prove more accurate. Davis and Seski[3] reported that 2 women of 46 years and 2 of 48 gave birth to children in over 50,000 deliveries at the Chicago Lying-in Hospital. Eastman[4] writes, "Pregnancy after the age of 47 is very rare. In 65,000 deliveries at the Johns Hopkins Hospital, only one such case is recorded and that in a feeble-minded colored woman who stated she was 49 but may not have known her correct age." The oldest known patient to be delivered at the Boston Lying-in Hospital reported her age to be 49.

Both the American and British literature reveal several instances of more advanced ages at time of delivery than those noted by the above-mentioned hospitals. These maternal ages were verified by reference to the mother's birth certificate. Gilbertson[5] records a woman 50 years and 7 months of age at birth of her last infant. Greenhill[6] states, "Both DeLee and Greenhill have delivered a woman of 52 years safely. . . ." Berkeley, Bonney, and MacLeod[7]

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write, "We have knowledge of 2 cases of pregnancy followed by normal labor in women in their fifty-first year, as verified by their birth certificates." It may be noted that a birth certificate is not of itself indisputable evidence of an individual's age. Occasionally birth certificates of deceased children have been mistakenly assigned to offspring born at a later date. This may occur when birth certificates have failed to name the child or in those cases in which a succeeding child was given the same name as a dead sibling who had earlier been registered.

The German literature contains numerous unproved cases of term pregnancies at advanced age. Lindpainter,[8] who reviewed the world literature prior to 1916, concludes that Kennedy's[9] is the only fully authenticated one in his series. Kennedy, who is similarly referred to in several American textbooks, reported a term pregnancy at 63 years of age in a gravida xxiii. Although the author was convinced of her advanced age, the evidence consists entirely of statements made to him by the patient: the fact that she was a nurse in his employ 10 years previously when she stated she was 50 and appeared to be of that age; and last, proof that 3 years earlier when her third husband applied to the local parochial board for relief he stated his wife's age to be 60. It can be seen that while the foregoing statements agree they do not provide unquestionable proof.

Except in cases involving interests in property, as mentioned, the current legal precedence is summarized by Glaister,[10] who states that the court held that a woman of 53 may or may not be sterile, and that the possibility of birth prior to the maternal age of 60 is to be determined individually in each circumstance.

The occurrence or absence of menstruation admittedly cannot be considered an indication of fertility. Pregnancy in apparently postmenopausal women under 50[11, 12, 13] is possible, as is irregular vaginal bleeding in the very elderly.

From what we have been able to gather from vital statistics and from medical literature, it appears that parturition in a woman over 52 years of age has not been proved, and that, therefore, were it surely to occur in a woman, say, of 55, it must be considered a gross aberration of reproductive physiology.

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245 POND AVENUE

FRUCTOSE AND FRUCTOLYSIS IN HUMAN SEMEN

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THE report of Mann[1] on fructose and fructolysis in the semen of bulls and their relation to fertility prompted this investigation of the metabolism of fructose in human semen.

Fructose is formed and secreted chiefly by the seminal vesicles and its formation is dependent on testicular hormone.[2] The initial fructose level is therefore an indication of the hormonal function of the testes. Mann regards the metabolism of fructose by the bull as a convenient measure of the metabolic activity of the bull's spermatozoa. In his studies on fructolysis of semen in a suitable phosphate buffer, the disappearance of fructose was steady and followed a linear course until the entire sugar content was exhausted. The rate of glycolysis in bulls' semen was correlated with the density and motility of the sperm. Azoospermic and necrospermic semen did not utilize fructose. A reduced rate of fructolysis was found in spermatozoa of poor motility.

Method

The technique described by Mann for the colorimetric determination of fructose in semen was adapted for the study of human semen and utilization of a Klett photoelectric colorimeter. Four-tenths cubic centimeter of freshly ejaculated human semen is pipetted into a narrow glass tube not more than 0.7 inch in diameter, followed by 0.2 c.c. of 0.25 phosphate buffer, pH 7.4.

One-tenth milliliter of the mixture is withdrawn and deproteinized immediately and the remainder incubated at 35 to 37° C. From the incubated mixture 0.1 ml. samples are withdrawn and deproteinized hourly for three hours.

Deproteinization is carried out in test tubes by diluting the 0.1 ml. of semen buffer mixture with 1.9 ml. of water. To this is added 1 c.c. of 2 per cent zinc sulfate and 1 c.c. of 0.1 N sodium hydroxide. These mixtures are then heated for one minute in boiling water and filtered. Two ml. amounts of the clear filtrate are measured into 10 c.c. Klett colorimeter tubes marked 0h, 1h, 2h, 3h.

To develop the color reaction, 2 ml. of 0.01 per cent alcoholic solution of resorcinol and 6 ml. of 30 per cent hydrochloric acid are added to each tube containing 2 ml. of filtrate. The tubes are then heated for 10 minutes in water at 80 to 85° C. and, after cooling, the determination is completed in the Klett colorimeter.

The color is read in a Klett colorimeter with a 54 green filter. Both the standard solutions and the semen extracts are read against a blank set at zero. The blank consists of 1 c.c. distilled water, 0.5 c.c. 2 per cent zinc sulfate, 0.5 c.c. 0.1 N sodium hydroxide, 2.0 c.c. of 0.1 per cent alcoholic solution of resorcinol and 6.0 c.c. of 30 per cent hydrochloric acid.

Calculation

Standard solutions of frutose were prepared containing 0.2 mg., 0.1 mg., 0.05 mg., and 0.025 mg. of fructose per cubic centimeter, and since the concentration of fructose is directly proportional to the readings on the colorimeter, a factor was established in determining the concentration of fructose in the semen samples. With the use of the factor, then, the application of the following simple formula would give the concentration of fructose in milligrams per cubic centimeter of semen.
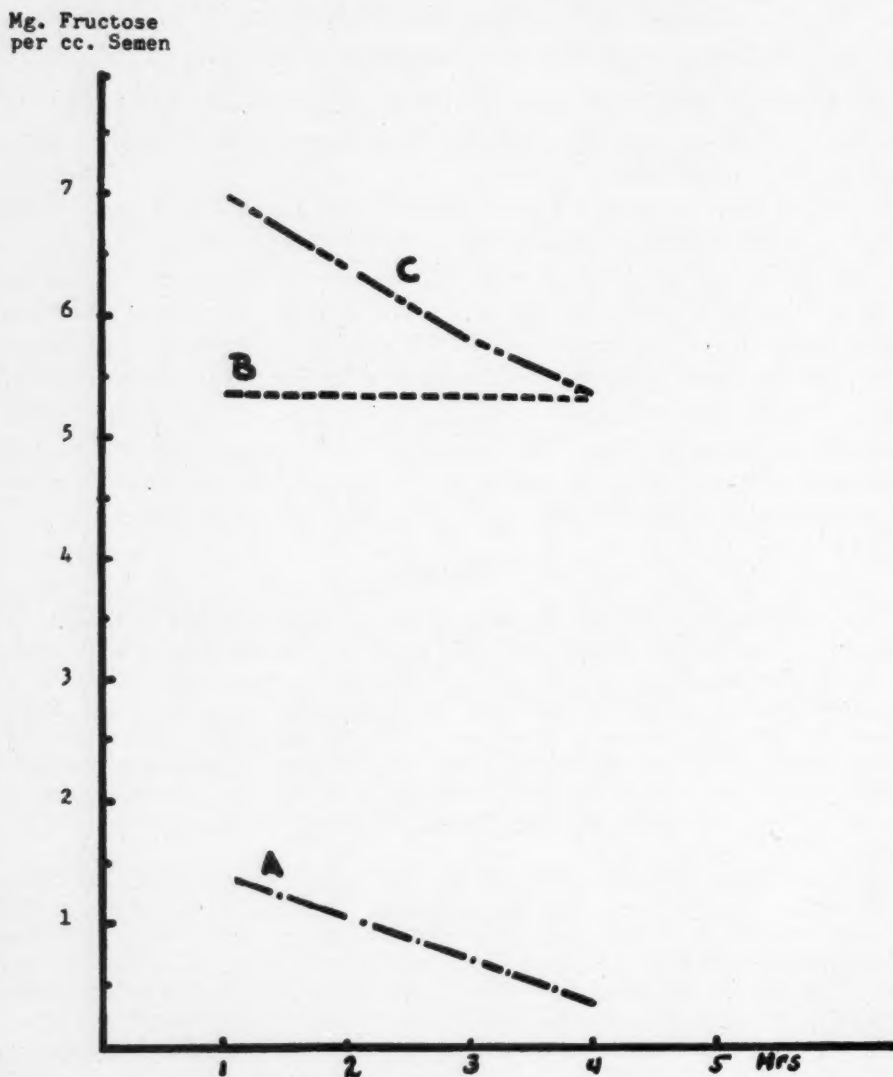

Fig. 1.—A—Count 83,000,000 sperm/c.c. Motility, 95 per cent.
B—Azoospermia.
C—Count 60,000,000 sperm/c.c. Motility, 30 per cent.

Factor X colorimeter reading × 30 equals milligrams of fructose per cubic centimeter of semen.

The most important detail in carrying out the determination is the maintenance of a constant pH in all portions of the specimens studied. Variation

in pH in different aliquots of the same specimen will result in marked fluctuations in the extent of fructolysis in each tube. For this reason the addition of an adequate buffer is essential.

Summary and Conclusion

Our preliminary studies with human semen parallel the results obtained by Mann with bulls' semen.[1] The rate of fructolysis is directly proportional to the number and motility of spermatozoa in the seminal fluid (Fig. 1).[2] The initial level of fructose in the seminal fluid is dependent on quality of this fluid and the freedom of pathology as regards its source.

Unfortunately, none of the specimens studied were freshly ejaculated so that no comment at this time can be made with regard to the initial fructose levels in fresh semen. However, our studies have indicated that in a vigorous, well-buffered specimen fructolysis follows a linear course.

Studies are in progress at present on the effect of testosterone medication on the fructose level of human semen and the effect of increased semen fructose on the survival time of spermatozoa. We are also studying fructolysis of human semen at different pH's approximating the acid pH of human vaginas and the effect of increased fructose in semen on spermatozoa survival under these conditions.

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THE RATE OF GROWTH OF UTERINE MYOMAS

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UTERINE myomas are the commonest of all human neoplasms, being present in approximately one-third of all women over 40 years of age.[5] The rate of growth of these tumors varies tremendously in different individuals. In the majority of cases growth is so slow that the myomas never attain clinical significance, nor are they even detectable on pelvic examination, being discovered only at operation for unrelated conditions or at autopsy. Occasionally myomas may grow so rapidly as to produce symptoms in early life, even before the age of 20 years,[2] or to result in tumors of tremendous size. In one extreme case, reported by Hunter,[3] the patient was host to a fibroid uterus which weighed 140 pounds.

Material

In this study an attempt has been made to obtain quantitative estimates of the rate of growth of myomas in a selected group of 32 nonpregnant patients. All were treated by hysterectomy some time after a previous pelvic laparotomy of known date, at which all visible myomas had been removed or their absence established. By utilizing the weight of the surgically removed tumors at the time of hysterectomy and the interval between operations it was possible to express the rate of growth of the myomas, according to the formula,

$$R = \frac{M}{t},$$

where M represents the weight of the myomatous mass in grams and t represents the time interval in years. All figures were taken to the nearest whole number.

The tumor mass was estimated from the weight of the surgical specimen, 60 grams being subtracted arbitrarily as the weight of the normal uterus (or 50 grams if hysterectomy was incomplete), and 5 additional grams for each ovary or tube. Parity of the patient was ignored in estimating the weight of the uterus itself, nor was any effort made to allow for the nontumorous uterine hypertrophy which results from the presence of myomas. The lack of precision in the results is therefore obvious.

In addition, the following assumptions have had to be made in calculating the growth rates, and it is quite probable that none of them is precisely valid:

First, that the myomas began to develop immediately following the first operation;

Second, that growth continued without interruption until hysterectomy;

Third, that the rate of growth remained constant.

The several qualifications imposed by these sources of error sharply limit the accuracy of the calculations. It is believed, however, that this approach does permit a crude estimation of at least the order of magnitude

of the rate of myomatous growth in the patients studied. The calculated rates must all be minimum values, because of the assumption that the tumor growth continued over the full time interval between the two operations. It is apparent also that the figures represent the rate of accretion of myomatous tissue to a single uterus, rather than the rate of growth of individual tumors. Thus, for the same time interval, identical rates would be obtained for a uterus containing a solitary myoma weighing 1,000 grams as for an organ with ten 100-gram tumors.

In the majority of cases the initial operation was a myomectomy. Although tiny undetectable seedling myomas may have escaped removal, their composite mass is assumed to have been so small as to have no significance for the immediate uterine weight. Multiple operative procedures were performed in many of the cases, but the tables list only what was considered the principal procedure in each patient. Average age refers to the mean of the ages at the two operations.

The calculated average rate of tumor growth for the entire group of 32 patients was 45.1 grams per year, ranging between the extremes of 1 and 225 grams per year. Table I presents the data for the 15 white patients and Table II the data for the 17 Negro patients.

TABLE I. RATE OF GROWTH OF MYOMAS IN WHITE PATIENTS

PATIENT	AVERAGE AGE (YEARS)	ORIGINAL OPERATION	INTERVAL, (YEARS)	HYSTEREC-TOMY SPECIMEN WEIGHT (GRAMS)	TUMOR WEIGHT (GRAMS)	MYOMA GROWTH RATE (GRAMS/ YEAR)
1	31	Suspension	26	200	120	5
2	35	Exploratory	21	125	55	3
3	35	Myomectomy	16	170	110	7
4	33	Myomectomy	6	270	210	35
5	34	Appendectomy	7	420	360	51
6	32	Oophorectomy	26	2,300	2,220	85
7	32	Oophorectomy	23	340	275	12
8	33	Myomectomy	6	270	210	35
9	39	Myomectomy	12	175	105	9
10	36	Myomectomy	12	470	420	35
11	33	Suspension	6	160	100	17
12	43	Partial hys-terectomy	8	140	130	16
13	42	Oophorectomy	17	80	15	1
14	32	Suspension	14	110	50	4
15	38	Suspension	29	500	420	14
					Average	22

The myoma growth rate in the white women averaged 22 grams per year, with a range of 1 to 85 grams per year. The average rate for the Negro group was 3 times as high, 67 grams per year, with a range of 2 to 225 grams per year. This difference is statistically significant.

No correlation could be established between the age of the patient and the rate of tumor growth.

The myomas on which this study was based probably had two different types of origin. Some were undoubtedly present but overlooked at the original operation. Others may have developed anew. Since it is clinically impossible to distinguish between the two types of growth, the term recurrence is used to denote the appearance of any myomas following myomectomy. Previous studies on recurrence of myomas have focused on the time interval before symptoms recurred, and in a few cases the size of the recurrent tumors has been recorded, either in linear dimensions[4] or in relation to the eggs of various species

of fowl.[1]   The present study, despite its lack of precision, has aimed at a more
quantitative measure of the range of growth rate of uterine fibroids.   Since the
patients under study comprised a small and selected group, any generalizations
concerning the biology of these tumors would be hazardous.   Nevertheless, the
data provide quantitative confirmation of their highly variable rate of growth
and of the clinical observation that the uteri of Negro women are particularly
fertile soil for myomas.   Fibroids have long been known to occur with greater
frequency in this race, and in this series of cases their rate of growth was 3
times that in the white patients.

TABLE II.   RATE OF GROWTH OF MYOMAS IN NEGRO PATIENTS

PATIENT	AVERAGE AGE (YEARS)	ORIGINAL OPERATION	INTERVAL (YEARS)	HYSTEREC-TOMY SPECIMEN WEIGHT (GRAMS)	TUMOR WEIGHT (GRAMS)	MYOMA GROWTH RATE (GRAMS/ YEAR)
1	31	Salpingectomy	9	370	310	34
2	37	Myomectomy	7	640	565	81
3	49	Myomectomy	8	85	15	2
4	34	Myomectomy	11	895	835	76
5	32	Myomectomy	6	205	145	24
6	39	Myomectomy	10	900	850	85
7	32	Myomectomy	6	1,400	1,350	225
8	36	Myomectomy	12	2,000	1,930	161
9	33	Myomectomy	10	480	420	42
10	27	Suspension	14	350	290	21
11	33	Myomectomy	5	380	320	64
12	40	Suspension	12	550	480	40
13	44	Suspension	7	1,220	1,140	163
14	24	Suspension	8	330	270	34
15	35	Sterilization	18	450	390	22
16	36	Myomectomy	24	660	580	24
17	38	Myomectomy	8	340	260	33
					Average	67

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TORSION OF NORMAL UTERINE ADNEXA*

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IT IS not uncommon to encounter a patient with an acute abdominal condition due to torsion of abnormal adnexa which were previously enlarged by inflammatory processes or neoplastic growths. However, it is rather unique to find it as a result of torsion of a normal ovary and Fallopian tube, neither of which was the focus of pre-existing pathology. Smith and Butler,[1] in 1921, reported 14 such cases, while Schute,[2] in 1932, was able to find only a total of 35 cases after an exhaustive search of the literature. In the ensuing 18 years, several additional cases have been described, mostly in the European and South American literature, but from the figures available it is obvious that torsion of the normal uterine adnexa is not a common phenomenon. This rare syndrome was found recently in three cases at the Beth-El Hospital in the relatively short period of two and one-half years. It merits reporting because of its infrequent occurrence, its obscure etiology, its complex differential diagnosis, and its unusual pathology.

CASE 1.—E. Z., aged 31 years, was admitted to the hospital on Jan. 5, 1947. She was a well-developed and well-nourished white woman whose previous pregnancy had terminated three years before with a normal spontaneous delivery of a living male child. Her past history and family history were essentially negative. Her menstrual history revealed a menarche at age 13 years with periods at irregular intervals of 6 to 8 weeks, lasting for 7 days. Severe dysmenorrhea was always present. Her last menstrual period was 28 days prior to the admission and was normal.

Twenty-four hours before admission, the patient began to experience intermittent pain in the right lower quadrant of the abdomen and continuous pain over the right kidney area. This pain radiated to the right groin and down the lateral aspect of the right thigh. It was accompanied by nausea, vomiting, and frequency of urination. The patient was admitted in acute distress.

Physical examination revealed a moderately obese abdomen which was slightly distended, tympanitic, and soft. There was slight tenderness to deep pressure in the right lower quadrant, but extreme tenderness on palpation of the right costovertebral angle. No masses were palpable. Pelvic examination disclosed normal external genitals, a multiparous introitus, and a seromucoid vaginal discharge. The cervix was firm, tender on motion, pointed upward toward the pubic symphysis, and was bluish and smooth with a closed external os on speculum examination. The uterus was slightly enlarged, retroverted, and fixed in the cul-de-sac. A normal left ovary was palpated in the left fornix anterior to the uterus. The right ovary was found to be enlarged to the size of an orange, irregular in contour, tender, and doughy. It occupied the right fornix and extended into the cul-de-sac. Rectal examination confirmed the pelvic findings.

Laboratory findings disclosed a negative urinalysis, hemoglobin of 72 per cent, red blood count of 4.2 million, white blood count of 13,800 with a differential of 86 per cent polymorphonuclear leukocytes and 14 per cent lymphocytes. The temperature was 99.0° F.,

pulse was 88, respirations 20, and blood pressure 104/64. Mazzini test was negative. Intravenous urography was normal.

A preoperative diagnosis of twisted cyst of the ovary was made and a laparotomy performed. There was free serous fluid in the peritoneal cavity with moderately distended small bowel. The uterus was slightly enlarged, retroverted, and normal in contour. The left ovary and Fallopian tube were normal. The right ovary and tube were twisted three times on their pedicle. They formed a bluish black edematous mass about the size of a small orange with multiple scattered dark hemorrhagic areas. The appendix was normal. A right salpingo-oophorectomy and appendectomy were performed. The patient made an uneventful recovery and was discharged on the eighth postoperative day.
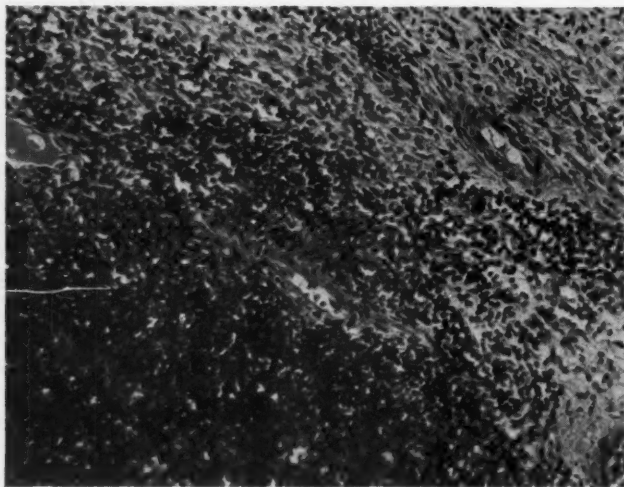
Fig. 1.

The pathological specimen consisted, grossly, of a thin-walled Fallopian tube which was patent throughout its length. The ovary was moderately enlarged and measured 6.5 by 5.0 by 2.5 cm. with its normal contour well preserved. On section, its cut surface showed marked edema with numerous punctate hemorrhagic areas. A prominent corpus luteum 2 cm. in diameter was present on its inferior border. Multiple serial sections of the ovary failed to reveal any gross neoplastic or cystic formation. The appendix was normal grossly. Microscopically, sections of the Fallopian tube and appendix were also normal. Multiple sections of the ovary (Fig. 1) showed parts of the ovarian stroma to be intact with normally stained stromal cells and numerous primordial follicles. The normal areas were sharply demarcated from an edematous and diffusely hemorrhagic zone in which erythrocytes were well preserved. No inflammatory or neoplastic changes were present.

The pathological diagnosis was torsion of a normal ovary and Fallopian tube.

CASE 2.—S. F., aged 10 years, was admitted to the hospital on April 5, 1949. She was poorly developed and malnourished. Her family history was noncontributory. The past history included a hospital admission two years previously for severe abdominal pain and vomiting. Physical examination and gastrointestinal x-ray series at that time were entirely negative. She was discharged with a diagnosis of chronic constipation. During the following two years, the patient's mother reported that she continued to have recurrences of the mild abdominal pain and vomiting which were relieved by almost daily enemas. A neurosis on the part of the patient was strongly suspected.

Eleven days before admission, the patient fell while skating and hurt her right side. This was soon followed by severe intermittent abdominal pain, nausea, and vomiting. There were no bowel or urinary difficulties. When the intermittent colic continued, it was deemed wise to admit the patient to the hospital for a complete work-up.

Physical examination revealed a thin young girl who complained of tenderness on palpation of the right costovertebral angle. Palpation of the abdomen elicited no tenderness and disclosed no masses. Because of the patient's age, vaginal examination was deferred. On rectal examination, an orange-sized mass was felt in the midline. It was nonmovable, solid, and tender. It was at first diagnosed as a congenitally retroverted uterus. On her second and third hospital days, the patient continued to complain of lower abdominal pain, especially during bowel movements. On the fourth day, she began to run a low-grade fever with a rapid pulse rate. The abdomen became very sensitive with rigidity in both lower quadrants. On the next day, a repeat rectal examination revealed that the previously fore-mentioned mass had grown to the size of a grapefruit, was semicystic, tender, and was now to the right of the midline.
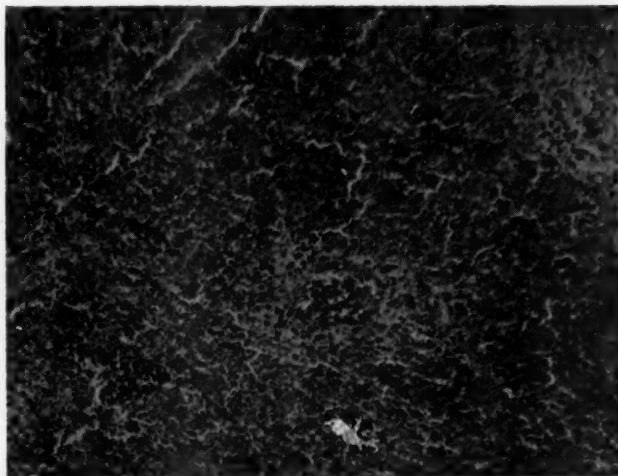
Fig. 2.

Laboratory findings disclosed a negative urinalysis, hematocrit of 45, red blood count of 4.2 million. The white blood count increased from 9,866 with 63 per cent polymorphonuclear leukocytes (April 6, 1949) to 20,000 with 82 per cent polymorphonuclear leukocytes (April 8) while the erythrocyte sedimentation rate increased from 16 mm./hr. (April 6) to 30 mm./hr. (April 8). The Mazzini test was negative. Intravenous urography was normal.

A preoperative diagnosis of twisted ovarian cyst was made on the fifth hospital day and a laparotomy performed. The uterus was found to be normal. The left ovary was cystic and enlarged to the size of a walnut. The right ovary and Fallopian tube formed a dark hemorrhagic and gangrenous mass about the size of a small grapefruit. The tube had made two complete turns around the ovary. The appendix was normal. A right salpingo-oophorectomy was performed. An uneventful recovery was made by the patient and she was discharged on the seventh postoperative day.

The pathological specimen consisted of a large ovoid ovary measuring 9 by 5 by 4 cm. with an attached tube 6 cm. long. The ovary was dark reddish black, smooth, and intact. On section, the cut surface was soft, edematous, red black, congested, and homogenous throughout. The tube was black, smooth, and unruptured. On section, its wall was homogenous, red black, and hemorrhagic. Microscopic sections of the ovary (Fig. 2) revealed little remaining intact stroma. Most of it had been transformed into a hemorrhagic and edematous mass with complete obliteration of all landmarks. In several areas, dense acute inflammatory reaction was seen. Multiple sections revealed no evidence of neoplastic or cystic changes.

The pathological diagnosis was torsion of a normal ovary and Fallopian tube.

CASE 3.—H. L., aged 33 years, was admitted to the hospital on Sept. 30, 1949. She was a well-developed and well-nourished white woman who had had one child nine years

previously. Her past history and family history were irrelevent. Her menstrual history revealed a menarche at age 16, periods occuring every 31 days, and lasting 5 days with no dysmenorrhea. Her last two periods occurred regularly on July 16, 1949, and Aug. 16, 1949, but were scanty and lasted only one day each.

Three days before admission, the patient began to experience intermittent colicky pains in the left lower quadrant of the abdomen which radiated to the back and down the left thigh. They were accompanied by nausea, vomiting, and a sensation of pressure on the left side. She was admitted in acute distress.

Physical examination revealed a tender abdomen with definite rebound tenderness in the left lower quadrant. There was no rigidity. A mass was palpated in the lower abdomen three fingerbreadths above the pubic symphysis. Pelvic examination revealed relaxed walls. The cervix was eroded and not tender to motion. The uterus was globular, softened, and enlarged to the size of a seven weeks' gestation. In the cul-de-sac there was a tender mass the size of an orange encroaching on the left fornix. The rectal examination corroborated the pelvic findings.
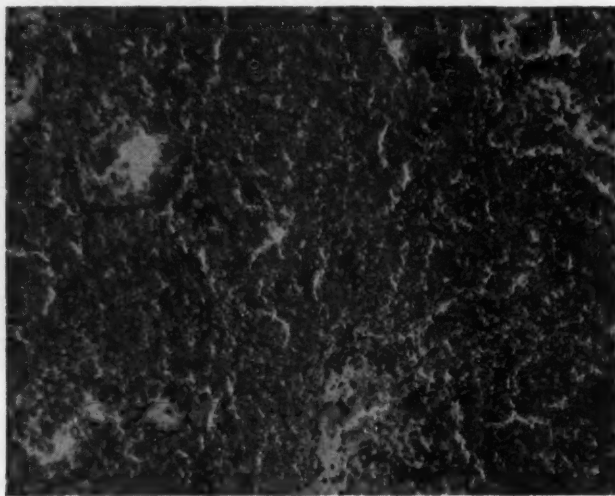
Fig. 3.

The laboratory report showed a negative urinalysis. The hemoglobin was 85 per cent; the white blood count was 17,200 with 80 per cent polymorphonuclear leukocytes, 16 per cent lymphocytes, and 4 per cent monocytes. The Mazzini test was negative.

The preoperative diagnosis was a twisted ovarian cyst complicating a seven weeks' intrauterine gestation. A laparotomy was performed. The uterus was found to be enlarged with a two months' gestation. Posterior to it, in the cul-de-sac, was an incarcerated mass the size of an orange which was the hemorrhagic left ovary with Fallopian tube, twisted four times on its pedicle. A left salpingo-oophorectomy was performed. The patient made an uneventful recovery and was discharged on the fourteenth postoperative day. The pregnancy subsequently proceeded to term.

The pathological specimen consisted of a hemorrhagic mass made up of the tube and ovary. The ovary measured 6 by 4.5 by 3 cm. Its surface was purplish red in color with focal areas of hemorrhage. On section the tumor was composed of a reddish black blood clot with smaller red areas scattered throughout. The tube measured 5 by 1.5 cm. Its surface was markedly congested and hemorrhagic. The lumen was dilated and filled with a blood clot. There was blood also present in the wall of the tube. Microscopically, little remained of the usual ovarian stroma (Fig. 3). An occasional shadow of a follicle was seen. The remainder of the ovarian stroma had been inundated with red blood cells. Sections through the tube revealed a retention of the basic architecture and preservation of the

epithelial lining of the mucosal villi. Extensive hemorrhage was present in the wall of the tube and there was marked dilatation of the subserosal veins. There was no evidence of cystic or neoplastic changes.

The pathological diagnosis was torsion of a normal ovary and Fallopian tube.

Comment

The three cases reviewed above represent a rare but important gynecological syndrome capable of taxing one's diagnostic acumen. It causes confusion because of its obscure etiology and lack of pathognomonic symptoms and signs. The predisposing cause is a persistence of the fetal state of elongation and tortuosity of the Fallopian tube.[3] The immediate cause is usually excessive abdominal strain. The important symptom is pain which varies greatly in intensity, increasing as the degree of torsion increases. It usually radiates along the ovarian nerves, following the ovarian vessels to the region of the kidney, and then pain is present in the costovertebral angle. Abdominally, tenderness and rigidity are usually present in variable degrees. On pelvic or rectal examination, a mass may be found closely associated with the uterus. The differential diagnosis includes such varied entities as mesenteric lymphadenitis, strangulated hernia, acute appendicitis, tubal pregnancy, acute salpingitis, ovarian neoplasms, and endometriosis.

The complications resulting from torsion of normal uterine adnexia include gangrene of the adnexa with spontaneous amputation from the uterus,[4] rupture of the ovary,[5] and thrombosis of the blood vessels of the pedicle with subsequent fatal embolization. The treatment is immediate laparotomy with excision of the involved adnexa.

Summary

Presented are three cases of torsion of normal uterine adnexa. This rare pathological entity is reviewed from the standpoint of its history, etiology, symptomatology, differential diagnosis, and complications. It occurs more often in adults because the supporting ligaments of undeveloped juvenile genital organs are so short and wide that the dangers of torsion are reduced to a minimum.[5] It is said to occur more often just before menstruation because of the increased congestion of the adnexa at that time. It probably occurs more frequently than we suspect. Despite its reported infrequency, this lesion should be considered in any female, regardless of age, who has pelvic and abdominal complaints.

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MALIGNANT SYNCYTIOMA FOLLOWING
BENIGN HYDATIDIFORM MOLE

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THE immediate treatment of hydatidiform mole offers no real problem to the obstetrician, evacuation upon diagnosis together with uterine curettage being generally accepted as the procedure of choice. The microscopic interpretation of this molar tissue and subsequent definitive treatment, however, remain debatable and subject to personal and geographic opinion.

Hertig[1] outlined certain measurable criteria in his classification of hydatidiform moles and concluded that there was a marked but not absolute correlation between the degree of apparent molar malignancy and the tendency for the patient to develop some grade of chorionic malignancy. The clinician could, therefore, by complete study of the mole and uterine curettings, be guided as to the necessity for subsequent hysterectomy.

In Hertig's classification an entity known as syncytial endometritis is described. It consists of an accentuation of the syncytial placental-site giant cells plus chronic infection and represents the lowest grade of chorionepithelioma, no cases with metastases having been reported. There were 9 such cases in Hertig's series but only 4 of these had originally been placed in the malignant group (Group VI) after study of the mole. Hertig further postulated that, if this entity is a true but very low-grade malignant tumor, representing an exaggeration of the picture seen in the normal placental site throughout pregnancy, it ostensibly might explain the rare choriocarcinoma that follows normal pregnancy (1:160,000), abortion (1:15,386), and ectopic pregnancy (1:5,333).[2]

The following case is of interest because of the development of an apparent chorionic malignancy within three months of evacuation of a Grade I (benign) mole and, further, because of the appearance of apparent chorionic pulmonary metastases which disappeared following hysterectomy and x-ray therapy.

Case Report

D. M., Cincinnati General Hospital No. 218247, a 25-year-old white para iv-o-i-iv, whose last normal menstrual period was Nov. 20, 1948, and whose estimated date of delivery was Aug. 27, 1949, was admitted to the gynecologic service on Feb. 17, 1949. Abdominal cramps and vaginal bleeding had been present for 4 days prior to admission and a diagnosis of threatened abortion was made. Her course in the hospital, however, was complicated by persistent vomiting, tachycardia, and fever, despite sulfonamides and penicillin. An obstetric consultant found the uterus to be approximately 18 weeks' gestational size despite a chronologic pregnancy of 12 weeks. The uterus was soft, symmetrical, and a fetal heart was not audible. The bleeding became prune juice in character and the vomiting increased. She was transferred to the obstetrical service with a diagnosis of hydatidiform mole.

Treatment consisted of hydration, mild sedation, penicillin, and vitamins. Clinical improvement occurred, but on March 11, 1949, vomiting, vaginal bleeding, and abdominal cramps recurred. The patient appeared acutely ill and complained of polyarthritis, weakness, and chills. The temperature was 100.4° F., hemoglobin 8.0 Gm., white cell count, 4,700. There was an erythematous dermatitis of the chest and arms. Electrocardiograms and x-rays of the chest were negative. A flat plate of the abdomen revealed no fetal parts, but the uterus seemed larger than on previous films. A Friedman test done on the cerebrospinal fluid was positive. A sterile pelvic examination revealed a long, uneffaced, undilated cervix. Cervical culture produced hemolytic staphylococcus in pure culture. Treatment was initiated with

penicillin, whole blood transfusion, hydration, and intravenous vitamins. Forty-eight hours later the temperature was normal and a dilatation and curettage were performed, a large hydatidiform mole being removed. Microscopic examination of the molar tissue and the curettings revealed the mole to be Grade I (benign) in type.

Another uterine curettage was done 6 days post evacuation because of persistent vaginal bleeding and a few fragments of trophoblastic tissue were removed. Microscopic examination revealed only necrotic decidua and a few hyalinized benign chorionic villi. A urinary Friedman test was positive on the day of curettage. Treatment was continued for 6 days with penicillin and sulfonamides and the temperature dropped to normal. The patient was discharged on the eighth postoperative day to be followed in the clinic with subsequent Friedman tests. The laboratory was not equipped to perform quantitative chorionic gonadotropin levels.
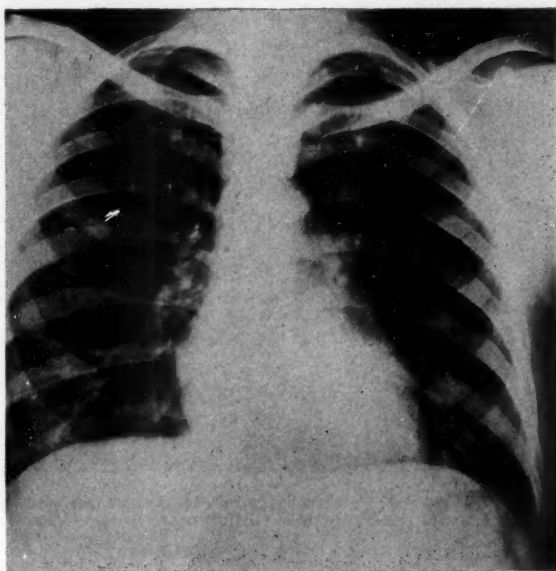
Fig. 1.—Photograph of chest x-ray showing round density in right third interspace interpreted as metastatic lesion.

The patient was readmitted 2 days following discharge because of excessive vaginal bleeding. Quantitative Friedman tests were negative, qualitative test positive. An x-ray of the chest was negative. Dilatation and curettage were performed on April 4, 1949, with removal of a few fragments of tissue. The microscopic report was "atypical hydatidiform mole." The patient was discharged, again to be followed in the Outpatient Clinic.

The patient did not return to the clinic but, on June 8, 1949 (6 weeks after discharge), she returned to the hospital complaining of (1) persistent vaginal bleeding; (2) abdominal pain; (3) cough; (4) bloody sputum. Examination revealed marked abdominal tenderness and rigidity. Pelvic examination revealed a long, thick cervix, with an irregular, doughy uterus. The temperature was 102° F., white cell count 14,000. X-ray of the chest revealed two definite round densities in the right third interspace (Fig. 1). Two previous chest films had been negative. It was the opinion of the radiologist that these represented metastatic lesions. A total hysterectomy was thereupon carried out on June 16, 1949. The uterus, when opened, showed a 2 by 2 cm. elevated, gray-purple nodule in the region of the right cornu. The microscopic report on a section taken from this area was "malignant syncytioma" (Fig. 2). (Diagnosis confirmed by Dr. Arthur T. Hertig.)

The immediate postoperative course was uneventful. X-ray therapy was initiated on the fifth postoperative day and the patient received 1,800 r over the right upper quadrant,

and was discharged on the twelfth postoperative day. An x-ray of the chest on July 5, 1949, revealed an approximate one-third decrease in the size of the nodular density. The patient was then seen at intervals of 6 weeks and remained asymptomatic. She was readmitted to the hospital in September of 1949 because of bronchopneumonia and responded rapidly to penicillin treatment. The lung lesion was markedly smaller on x-ray examination (Fig. 3).

An x-ray of the chest in tumor clinic on Nov. 30, 1950, revealed no evidence of disease. The patient was well and gaining weight.

At the time this report is written the patient remains asymptomatic and without x-ray evidence of disease.
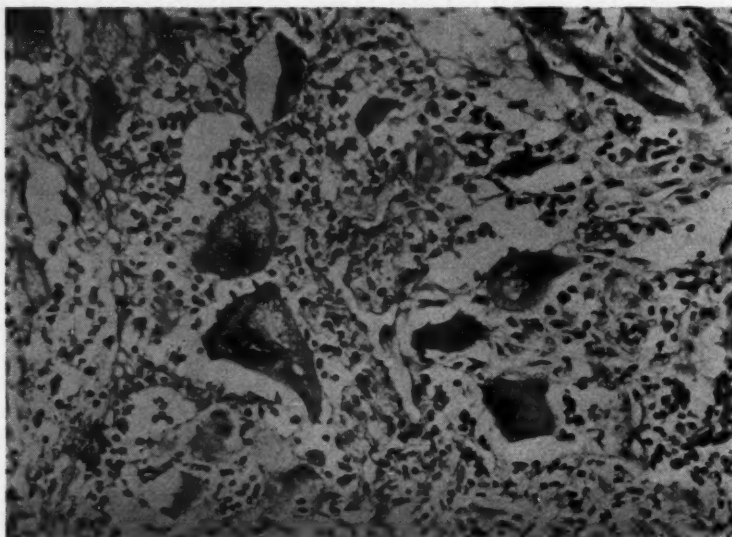
Fig. 2.—Photomicrograph of residual uterine lesion showing malignant-appearing syncytial giant cells and chronic inflammatory process.

Comment.—This case demonstrates well the possibility, rare though it may be, of the development of chorionic malignancy following evacuation of a benign hydatidiform mole. The tissue making up this tumor would seem to be the malignant counterpart of syncytial endometritis, indeed, a malignant conversion of the intrinsically invasive syncytial cells of the implanting ovum into neoplastc cells capable of growth following transporation to a new organ site.

This tumor may then be considered as an interval stage between syncytial endometritis and choriocarcinoma, that is, one in which merely a part of the fetal tissue (syncytial element) has undergone malignant transformation, whereas in the true chorionepithelioma of Marchand, both cytotrophoblast and syncytiotrophoblast are represented. It may be speculated further that possibly the syncytial elements are more radiosensitive, or more easily destroyed by the innate defense mechanisms of the recipient tissue.

The rationale of early hysterectomy following expulsion of a hydatidiform mole of Grade IV through VI is still questioned by many authors, despite the fact that in Hertig's series, 47 chorionic malignancies followed the 115 cases in these groupings (40.8 per cent). The majority of these were classified as chorioadenoma destruens (32 cases) whereas only 5 were diagnosed true chorionepitheliomas. There seems to be a marked discrepancy, however, in the cure rate of the two entities, 97 per cent survival (1 death from sepsis) in chorioadenoma destruens and 0 per cent survival in the chorionepitheliomas. Although Ewing[3] has stated that all patients characteristically succumb to the latter disease, perhaps the difference may be found in the treatment employed. Twenty-seven of the patients having chorioadenoma

destruens had hysterectomies (4 had insufficient data regarding treatment) whereas 4 of the 5 patients with chorionepithelioma died with the uteri intact, the fifth not being removed until just prior to death.

In view of the increasing number of cases being reported describing apparent two- to three-year survival after early hysterectomy for choriocarcinoma either with or without pulmonary metastases, it may be questioned as to whether early hysterectomy following expulsion of an apparently malignant mole (Grades IV through VI) might not be the procedure of choice. Park and Lees,[4] in reviewing 516 cases of reported choriocarcinoma, found 12 cases of regression of pulmonary metastases. In only 4 of these, however, was there roentgenographic evidence of such regression. Maier and Taylor[5] described a patient with a
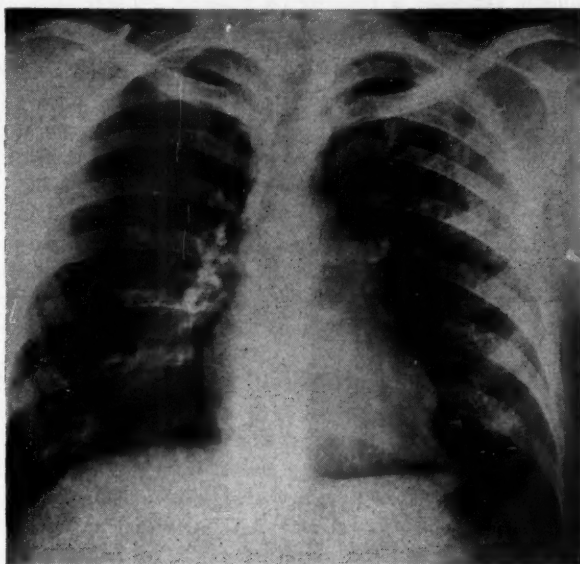
Fig. 3.—Photograph of chest x-ray 3 months postoperatively showing almost complete disappearance of pulmonary lesion.

solitary pulmonary metastasis of choriocarcinoma occurring two and one-half years after passage of a hydatidiform mole. This lesion was removed by lobectomy, confirmed microscopically, and resulted in evident cure. Johnson[6] has recently reported a two-year "cure" following hysterectomy, the pulmonary lesions regressing without irradiation. Siegler and associates[7] noted 11 cases of choriocarcinoma and one destructive mole with survival in 6 patients. Although there is some question as to the validity of the histologic diagnosis in several of these cases (comment by Arthur T. Hertig[8]), the fact remains that immediate hysterectomy is recommended for choriocarcinoma together with surgical removal or irradiation of metastases. In this latter series, 2 of the 6 patients who died did not have hysterectomies and another 3 had delayed hysterectomies.

The author is inclined to agree with the recent discussion by Hertig[8] to the effect that following molar curettage of probable malignancy, in a woman over 35 of moderate parity, early hysterectomy is the procedure of choice. In younger patients of less parity the proper therapy is indefinite and will depend upon histopathology and clinical course. Even here, in certain instances, radical treatment together with surgical or radiation therapy for metastasis may be indicated.

Conservatively speaking, it may be argued that 60 per cent of these women will not develop chorionic malignancy and numerous normal uteri will have been sacrificed. Yet, at the moment, there is no way of predicting from examination of the molar curettings which patient will have no further difficulty and which will proceed to local or distant trophoblastic proliferation and invasion.

Summary and Conclusions

1. A case of malignant syncytioma following a benign hydatidiform mole is reported.

2. Apparent pulmonary metastases from this chorionic malignancy resolved following hysterectomy and x-ray therapy.

3. The question of early hysterectomy following expulsion of malignant moles is discussed.

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245 POND AVENUE

DONOVANOSIS OF TUBES AND OVARY TREATED WITH AUREOMYCIN AND SURGERY

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GRANULOMA inguinale, or donovanosis,[1] as we prefer to term it, is a specific infection characterized by granulomatous lesions and is caused by *Donovania granulomatis*,[2,3] a gram-negative bacillus commonly known as the Donovan body. Despite the fact that most coital partners of patients with these lesions escape infection, the disease is considered to be venereal in nature. Though not a rare disease—Greenblatt[4] estimates that there are 5,000 to 10,000 sufferers of the infection in the United States—invasion of the tubes and ovaries by the organism is a decidedly uncommon occurrence. We were able to find only 6 cases of the condition in the literature.[5-9] All of the 6 patients died of this or an associated disease.

There is reported here a case of donovanosis involving the external and internal genitals. The patient was successfully treated both medically and surgically, and, after 5 months, is well and symptom free.

A 30-year-old Negro woman, para 0, gravida 0, was admitted to the gynecological service of the Harlem Hospital with the chief complaint of pains in the lower abdomen of 5 days' duration. Her present illness began 1 month before hospitalization when she had 2 episodes of vaginal bleeding, the most recent one occurring 12 days before admission, lasting 3 days. Five days prior to admission, she developed vertigo and pains in the lower part of the abdomen. There was no fainting. Treatment by her local physician with penicillin brought about no amelioration of the symptoms, and she was referred to the hospital for diagnosis and treatment.

Physical examination revealed a thin Negro woman in some distress with a temperature of 101.6° F., pulse 96, blood pressure 120/90, and a rapid sedimentation rate. The skin was warm and dry. The abdomen was tense, but there were no masses palpable nor rebound tenderness. The external genitals revealed a flat, sessile, irregular, nonfriable lesion at the posterior fourchette. The lesion was moist and confluent with a larger lesion on the medial aspect of the left buttock. Vaginal examination revealed a roomy vagina. The cervix was in the body axis, freely movable, firm, and nontender to motion. Speculum examination revealed bilateral cervical lesions similar in appearance to the external lesions. The fundus was difficult to outline, but did not appear to be enlarged. Both adnexa were tender with a sensation of fullness bilaterally. A cystic mass, difficult to outline in its entirety, was felt on the left side. Rectovaginal examination confirmed the presence of a cystic mass on the left side that was closely applied to the uterus, and rose to 3 fingerbreadths below the umbilicus. There was also a thickening of the right fornix.

A preoperative diagnosis of tubo-ovarian abscess was made, and the patient was operated upon one week after admission. The findings were as follows: The uterus was grossly normal in appearance except for 3 small, subserous myomas. There was a large tubo-ovarian abscess on the left side measuring 9 by 5 by 5 cm. It was fluctuant, thin, and closely adherent to the body of the uterus. On the right side there was a relatively large pyosalpinx that was prolapsed into the pouch of Douglas. The surrounding ovary was apparently uninvolved. A left salpingo-oophorectomy, right cornual resection, and multiple myomectomies with a 1-point suspension of the uterus were done.

The pertinent laboratory findings were: Dark-field examination of vulval and cervical lesions was negative, as were the Frei test and smears and cultures for *Neisseria gonorrheae*.

Tissue smears from the vulval and cervical lesions showed *Donovania granulomatis*. Subsequently, Giemsa-stained tissue sections from the tubo-ovarian specimen excised from the patient also revealed this organism within mononuclear cells (Fig. 1).

The patient was subjected to aureomycin therapy consisting of 1 Gm. orally, twice daily. Seven days postoperatively there was almost complete epithelization of the vulval lesion, and the smears were negative for Donovan bodies. The cervical lesions, though still present, were healing, and smears were negative for Donovan bodies. When the patient was re-examined for discharge from the hospital on the fifteenth postoperative day, there was no evidence grossly of any lesion of the vulva or cervix. She had received a total of 29 Gm. of aureomycin, orally.

Examination on her last visit, 5 months postoperatively, showed no evidence of recurrence of the disease.
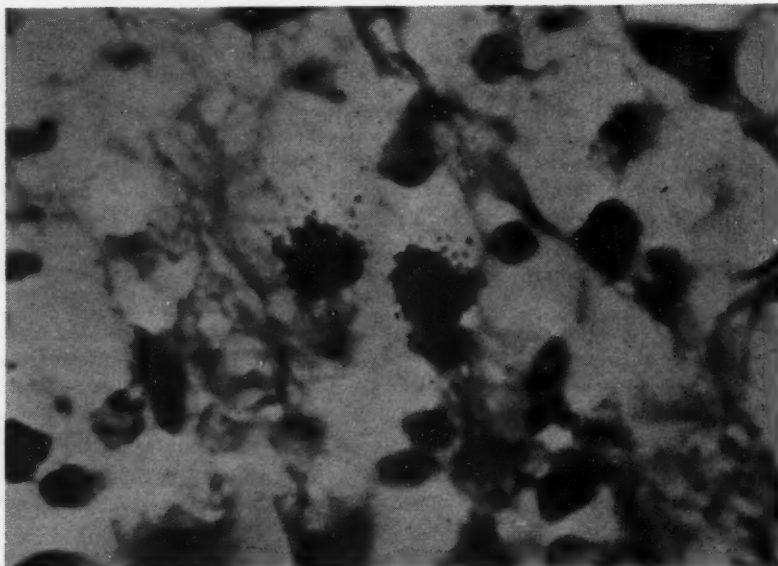

Fig. 1.—Photomicrograph of section of ovary showing Donovan bodies.

Comment

Donovanosis of the tubes and ovaries, judging from published reports, is extremely rare. We were able to find only 6 cases in the literature, 4 of which were reported from the laboratories of the Georgia University School of Medicine[5, 6, 7] where donovanosis is extensively studied, and where the workers are on the alert for the disease. On the other hand, we have reports of patients in whom donovanosis of the adnexa is strongly suggested, but not confirmed. Lyford, Scott and Johnson[10] reported a case of donovanosis manifested by arthritis and osteomyelitis in a 29-year-old woman who also complained of lower abdominal pains. She was treated with tartar emetic. Rhinehard and Bauer[11] reported a case of skeletal donovanosis in a patient who had previously had a hysterectomy and bilateral salpingo-oophorectomy. A somewhat similar case was reported by Lipp and Bibby.[12] In view of the disseminated nature of the disease, there is the temptation to ascribe the abdominal pathology in these cases to invasion by *D. granulomatis*.

Diagnosis.—The definitive diagnosis of donovanosis of the adnexa can be made by Giemsa stain of these tissues removed at operation or autopsy. In the absence of surgical intervention, the diagnosis of donovanosis in these organs can only be inferred by the demonstration of D. granulomatis in more accessible lesions (cervix, vulva, etc.).

In our case the diagnosis was suspected when Donovan bodies were found in the vulval and cervical lesions, and definitely established upon microscopic examination of the surgical

specimen. The presence of donovanosis in the right tube which was not removed can only be inferred.

At Harlem Hospital we have encountered no undue difficulty in finding *D. granulomatis* in giemsa-stained smears or sections. We find that the hematoxylin and eosin stain is unsatisfactory for the purpose, and we have found no histological cellular changes specific for this disease.

Treatment.—The antibiotics have now replaced the less effective antimony compounds as the treatment of donovanosis.

In 1946, Barton, Craig, Schwemlein, and Bauer[13] reported that streptomycin showed excellent results in 3 cases of donovanosis. This was confirmed by Greenblatt, Dienst and Kupperman.[14] In 1948, Wright, Sanders, Logan, Prigot, and Hill[15] of this hospital showed that aureomycin healed lesions of donovanosis, and suggested its use because of the lower toxicity and ease of administration as contrasted with those of streptomycin. Chloramphenicol was found to be effective by Greenblatt, Wammock, Dienst, and West[16] in 1949. Terramycin was used in single cases each by Hendricks, Greaves, Olansky, Taggart, Lewis, Landman, MacDonald, and Welch[17] and by Schoch and Alexander,[18] and in a somewhat larger series by Whitaker, Wright, Beinfield, Wilkinson, and Marmell.[19]

The treatment of donovanosis in patients in whom the disease has brought about pathological changes unresponsive to or irreparable by the antibiotics alone must be associated with surgical intervention. The judicious use of surgery with antibiotics is the best treatment for the far gone, neglected cases.

The treatment of our case presented a problem. The patient had obvious pelvic pathology, the origin of which could be ascribed either to the known donovanosis or to the more common causes of adnexal disease. Tubo-ovarian abscess, unlike pyosalpinx, does not respond well solely to antibiotic therapy. Though it may go on to tubo-ovarian cyst and become quiescent, it is usually expected to remain in abscess formation, relight at any time, and eventually require surgical treatment. For this reason laparotomy was decided upon. Because of the patient's age, it was decided to spare the right adnexa and do a cornual resection of the right Fallopian tube to prevent the possibility of future reinfection by way of the genital tract.

The vulval and cervical lesions and the pyosalpinx, which we infer was caused by *D. granulomatis*, were treated with aureomycin. Whether antibiotic therapy alone would be effective in reducing and eradicating a tubo-ovarian abscess due to *D. granulomatis* is not known.

Summary

A case of donovanosis involving the vulva, the cervix uteri, both Fallopian tubes, and the left ovary is described. The condition was treated by surgical removal of the left tubo-ovarian abscess and by the administration of aureomycin for the remaining pathology.

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OVARIAN PREGNANCY, WITH REPORT OF A CASE

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CASES of true primary ovarian pregnancy are being reported more and more frequently in the literature. Novak's[1] estimate of approximately 50 acceptable cases as of 1940 must surely be revised upward by now. The known incidence is of course low. At St. Luke's Hospital in New York, 339 cases of ectopic pregnancy included one ovarian pregnancy, the incidence in this series being 0.29 per cent.[2] Young and Hawk[3] state that ovarian pregnancy occurs approximately once in every 25,000 pregnancies.

It is known that the ovum as it exists in the ovary is incapable of fertilization until it has undergone certain maturation changes which are completed only during its passage through the tube. This fact makes it difficult for one to accept the old belief that conception might actually occur in the ovarian follicle itself. Present opinion seems to favor the theory that the ovum is discharged from the ovary, fertilized in the tube, and then for some unknown reason is discharged back into the peritoneal cavity and then implanted on the cortex of the ovary or even in a ruptured follicle. Meyer asserts that the cortical implantation is the more common mechanism.

The patient was an 18-year-old nulligravida admitted on April 1, 1950, with the chief complaint of pain in the abdomen and fainting. She was perfectly well until the morning of admission. While out walking she became nauseated, went into a friend's house, and vomited. Immediately following this she became aware of a sharp pain in the right lower quadrant. Soon after this she fainted. During the next two hours she fainted twice again, the right lower quadrant pain became more severe, and she developed pain in the right shoulder. By this time she had called her physician and he admitted her to the hospital. Menstrual history was entirely normal. She had a 25-day cycle and was quite regular. Her last menstrual period was on March 5, 1950, making the day of the onset of her present illness the expected time for her next period. She was quite definite about her last menstrual period being perfectly normal. Her previous menstrual period had been on Feb. 10, 1950. For the week prior to admission she had noted breast tenderness and enlargement as well as morning nausea. She had had no fever or chills, no urinary symptoms, and no bowel dysfunction. There had been no previous similar episodes. She had had an appendectomy at the age of 11 years. She had been treated for a "pelvic infection" two years before with douches. She had been married 2½ years and had used no contraceptives.

On admission to the hospital her blood pressure was 100/50, pulse 104, respiration 32, and temperature 97.2° F. Physical examination revealed a well-developed, well-nourished white woman who was quite pale. The extremities were cold. The breasts were slightly enlarged and tender. The heart and lungs were clear. Examination of the abdomen revealed definite lower abdominal tenderness, worse in the right lower quadrant. There were 2 plus rebound tenderness and dullness to percussion across the lower abdomen. There were no masses. Bowel sounds were diminished. There was one to two plus rigidity. Pelvic examination revealed essentially normal external genitals and vagina. The cervix was bluish, soft, and exquisitely tender to motion. There was no bleeding. Bimanual examination was almost impossible because of tenderness. One examiner thought that he felt a mass in the right adnexa. The cul-de-sac was "boggy" in consistency.

Laboratory work revealed a negative urinalysis (catheterized specimen). The hematocrit was 37, the hemoglobin 11.6 Gm. and the white blood count 13,000.

A preoperative diagnosis of a ruptured right tubal pregnancy versus a twisted or bleeding ovarian cyst was made. A transfusion was started and the patient taken to surgery for laparotomy. The abdomen, when entered, was found to contain a large amount of old and fresh blood. Examination of the pelvic organs revealed a slightly enlarged and softened uterus. Both tubes were entirely normal. The left ovary appeared small and atrophic. The right ovary contained a thin-walled cyst measuring approximately 2 inches in diameter at one pole. Adjacent to this was a cavity from which active bleeding was occurring. Partially plugging the opening of this cavity was a spherical mass of tissue grossly resembling chorionic villi. This mass of tissue measured approximately ¾ inches in diameter. A right salpingo-oophorectomy was performed without difficulty. A total of approximately 1,000 c.c. of blood was removed from the abdomen during the operation. She was given 1,000 c.c. of blood. The postoperative course was uneventful.
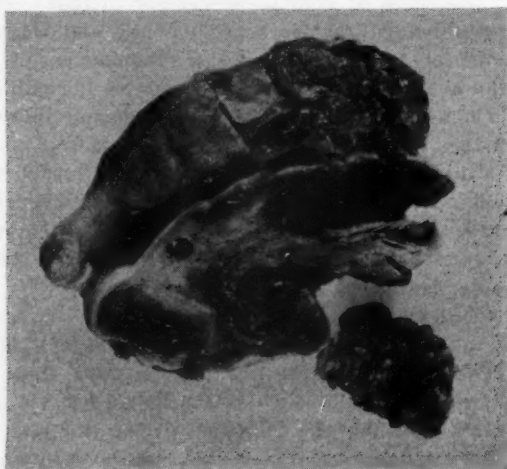

Fig. 1.—Picture of gross specimen. The ovary has been cut sagittally. The young corpus luteum is seen at the left pole of the ovary and the evacuated old corpus luteum cyst at the right upper pole. The cavity between the two represents the gestational sac with the expelled villous plug adjacent to it.

The Specimen.—

Gross: Excised right ovary and attached segment of Fallopian tube received. The ovary measured 4½ cm. in length by 2½ cm. in diameter. One pole of the ovary was occupied by what was apparently a previously ruptured cyst. This cyst measured 1.3 cm. in diameter. Its lining was smooth and shiny. Adjacent to this was another cavity measuring 1.5 cm. in diameter. In the lining of this cavity were what appeared to be chorionic villi. The wall was hemorrhagic in character. The remainder of the surface of the ovary was grayish-pink with small follicle cysts visible up to 6 mm. in diameter. The ovary was transected longitudinally. This revealed at the opposite pole of the ovary an intact corpus luteum measuring 1.2 cm. in maximal diameter. A microscopic section was taken.

The Fallopian tube had a maximal diameter of 1.3 cm., appeared slightly hemorrhagic, and was unattached to the ovary except by its mesenteric ligament. Representative sections were taken.

Also received was one globule of villous tissue and blood clot, measuring 2 by 1.5 cm. The fetus could not be identified in this structure.

*Microscopic.—*Section one: Expelled villuslike tissue. This section showed an active chorionic villous structure and portion of the amniotic sac. The trophoblastic activity was

as would be expected in early gestation, moderately active. Two layers of cells were seen on the chorionic villous structures. There was little, if any, vascularization in the core of the villi.

Section two: Uterine tube. Section of the uterine tube revealed no decidual reaction and only a slight degree of edema of the wall and the mesosalpinx.

Fig. 2.—Photomicrograph showing invasion of ovarian tissue by chorionic villi and trophoblasts.
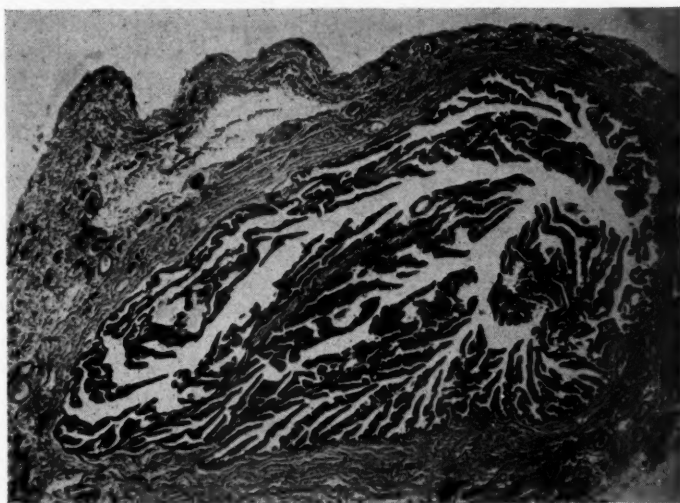

Fig. 3.—Cross section of Fallopian tube showing normal tubal structure without any evidence of pregnancy.

Section three: Sagittal section of ovary. At one pole of the ovary was seen a well-developed corpus luteum. Between this and the gestational sac lay normal ovarian tissue, including the hilus of the ovary. The gestational sac was represented by a large cavity filled with chorionic villi and blood clots. At one extreme edge of the cavity corpora lutea cells were seen. The remainder of the lining of the cavity consisted of ovarian stroma being invaded, in some places rather deeply, by trophoblastic cells. Inferiorly and laterally to the gestational sac was seen a portion of the lining of a cyst. This represented an old corpus luteum cyst. The wall was made up mainly of fibrous tissue with a moderate number of degenerating lutein cells.

In the remainder of the ovary numerous follicle cysts and several corpora albicantia were seen. The follicle cysts were small, but in several the granulosa cells were showing a definite hyperplasia and ballooning out of their cytoplasm so that in some respects they resembled a reaction seen in a corpus luteum.

Comment.—This particular case meets all of the criteria set up by Spiegelberg[4] for a true primary ovarian pregnancy. These are: (1) The tube, including the fimbriated end, must be distinctly separate from the ovary; (2) the gestational sac must definitely occupy the normal position of the ovary; (3) the gestational sac must be connected with the uterus by the uterovarian ligament; (4) unquestionable ovarian tissue must be demonstrable in the walls of the sac. It also meets the requirement asserted by Norris[5] that the tube must show no microscopic evidence of pregnancy. Because of the rather extensive invasion of this ovary by the pregnancy it is rather difficult to classify this case as either an intrafollicular or juxtafollicular ovarian pregnancy. The finding of old lutein cells along one edge of the gestational sac rather favors the former.

We are greatly indebted to Dr. Emil G. Holmstrom, Professor of Obstetrics and Gynecology, University of Utah College of Medicine, who examined and described the gross and microscopic pathology for us.

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508 EAST SOUTH TEMPLE

NONFATAL MATERNAL PULMONARY EMBOLISM BY AMNIOTIC FLUID

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IN 1941 Steiner and Lushbaugh[1] reported eight cases of maternal pulmonary embolism by amniotic fluid and thus introduced a previously unrecognized complication of pregnancy. Since then, these authors[2, 10] have added three more cases. In the past four years, other writers have contributed twenty-four[3-20] additional fatal cases, making a total of thirty-five patients in whom this entity was discovered at autopsy. Some of these cases were brought to light only by a review of autopsy material of patients who died in the last trimester of pregnancy, in labor, or in the early postpartum period.

In 1947 Seltzer and Schuman[21] reported an acceptable case of nonfatal maternal pulmonary embolism in which amniotic fluid was believed to be the offending substance.

The case herein reported is the second report of a nonfatal case of maternal pulmonary embolism in which amniotic fluid is considered to have been the cause. It is hoped that the clinical picture as described, with x-rays and other laboratory data, may aid others in recognizing this condition as a clinical disease entity.

Case Report.—M. A., a 24-year-old white Portuguese primigravida, had always been in good health. Her last menstrual period was Feb. 10, 1950, and delivery was expected on Nov. 17, 1950. Her prenatal course was uneventful. On Nov. 14, 1950, x-ray pelvimetry showed the pelvis to be android in type with average measurements and converging side walls. The fetal head was in the inlet.

At 1:00 A.M. on November 26 after 41 weeks of gestation she spontaneously went into labor. She was admitted to the hospital at 4:19 A.M. in mild labor. The membranes ruptured spontaneously at 7:45 A.M. and pains began to occur every 2 to 3 minutes until full dilatation was reached at 8:00 P.M. After two hours in the second stage of labor the head was molded well down in the midpelvis in the left occiput transverse position. At 10:27 P.M. after 21½ hours of labor, a living, 9 pound, 2 ounce (4,139 grams) male infant was delivered by Elliott midforceps aided by a deep right mediolateral episiotomy which extended well up the right lateral wall. Moderately hard traction was required for delivery of the head and shoulders. The baby was in some distress and there was a moderate amount of vernix caseosa and meconium in the amniotic fluid. The uterine bleeding was within normal limits and there was moderate bleeding from the episiotomy. The patient was given 1 c.c. Pitocin and 1 c.c. Ergotrate intramuscularly. The baby's condition improved rapidly with oxygen.

The premedication had been 0.8 Gm. Seconal and 150 mg. Demerol in divided doses given during active labor. Anesthesia was nitrous oxide-oxygen and then ether. Induction was smooth and there was no vomiting or coughing at any time. As she recovered from the anesthesia she complained of being cold. The respirations were rapid and her color was a little dusky but as her blood pressure was 116/78 and the strength of pulse was normal, she was sent to the recovery room. Approximately one hour after delivery it was noted that her condition was very poor. The respirations had increased to 70 per minute, she was deeply cyanotic, the pulse was weak and at times absent, and the cardiac rate had risen to 160. She was restless, orthopneic, and thrashing about in an effort to breathe. She became irrational and then semicomatose. She had no chest pain and there was only an occasional dry cough. Examination of the lungs revealed bilaterally equal, but slightly diminished, breath sounds at the bases, vesicular throughout and there were no r$\hat{a}$les of any type. Cardiac action was perfectly regular with tachycardia. There were no signs of cardiac enlargement. No murmurs were heard. There was no enlargement of the liver and no marked venous engorgement in the neck. A clinical diagnosis of pulmonary embolism by amniotic fluid was made.
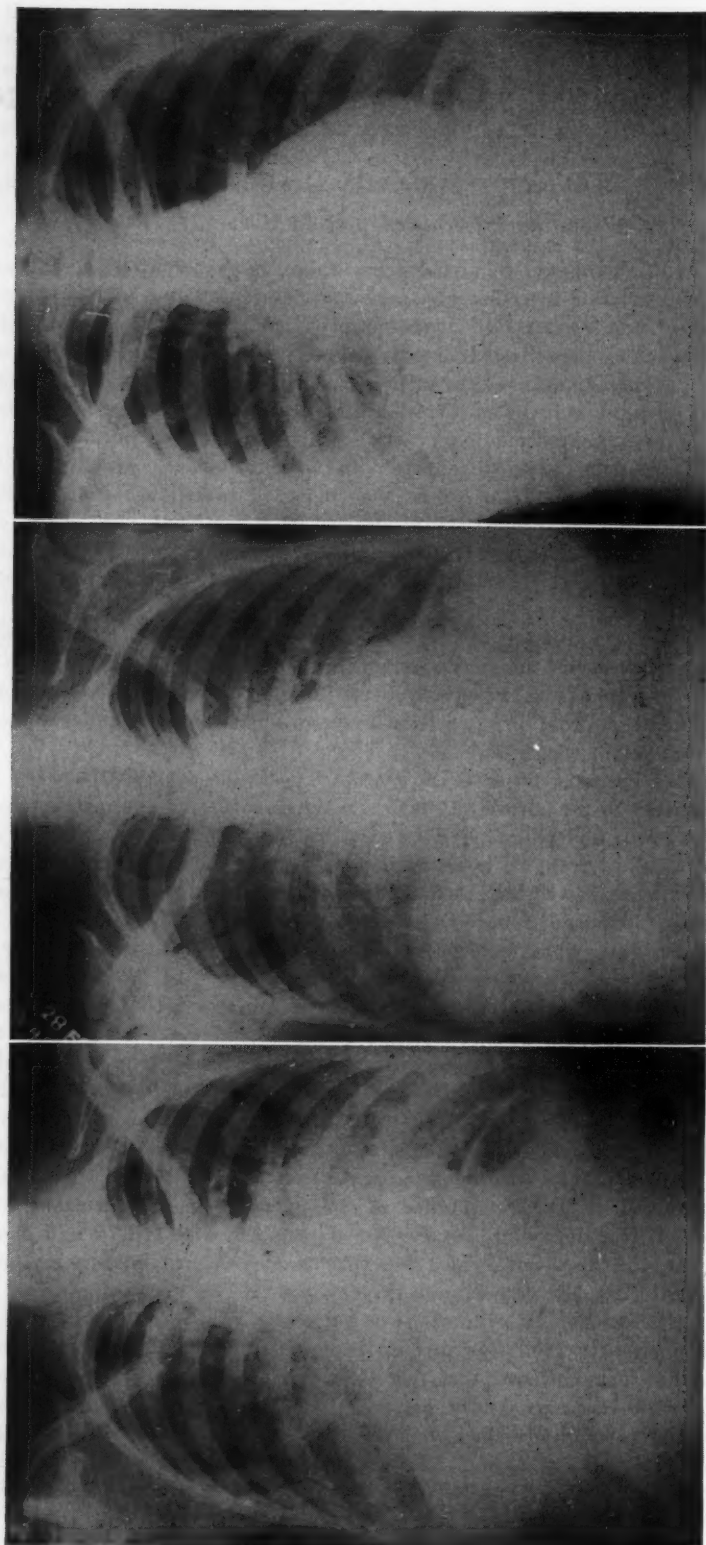
Fig. 1.—X-ray of the thorax 4 hours after delivery.
Fig. 2.—X-ray of the thorax 33 hours after delivery.
Fig. 3.—X-ray of the thorax 6 days after delivery.

Oxygen by face mask was given but it was difficult to keep the rebreathing bag filled because of the rapid respirations. As soon as possible she was shifted to 100 per cent oxygen by a positive pressure mask. Aminophylline, 0.5 Gm. by rectal suppository, was given. Her color gradually improved and she regained consciousness and the pulse became stronger.

It was decided to risk transfer of the patient for immediate chest x-ray and electrocardiographic study. She was transported in an upright position with positive pressure oxygen to the Rhode Island Hospital where the studies were taken at 2:45 A.M. The chest x-ray (Fig. 1) shows extensive density fanning out from both hilar regions and extending into the periphery of all lobes. This is most marked in the basal halves of the lung fields, but it extends up into both apices. There is no consolidation or free effusion. The heart shadow shows no enlargement or abnormality of contour. The domes of the diaphragm occupy normal levels and there are no signs of pulmonary atelectasis. The appearances are similar to those seen with marked pulmonary vascular congestion.

An electrocardiogram showed a rapid regular rhythm due to sinus tachycardia with a rate of 150 beats per minute. The QRS complexes were of normal duration and in the limb leads showed right axis deviation. There was a deep S wave present in Lead I and some flattening of the T wave in Lead II. In Lead III there was a Q wave with slight elevation of the ST segment and inversion of the T wave. Exploring chest leads showed the presence of a deep S wave in the fifth position and a small one in the sixth. The electrocardiogram was interpreted as quite suggestive of acute cor pulmonale.

Approximately three hours after the onset of her illness, the blood pressure was 84/60. The pulse rate was 150, the temperature was 102.6° F. by rectum, and respirations were 60. She experienced some substernal discomfort on the few occasions that she coughed.

The patient was given 0.5 Gm. of aminophylline by rectal suppository every 4 hours and she frequently asked for the suppositories to be given more often. They seemed to aid her respirations considerably. Four hundred thousand units of penicillin were given intramuscularly daily. The white blood count was 16,400 per cubic millimeter with 90 per cent polymorphonuclear leucocytes, 8 per cent lymphocytes, and 2 per cent monocytes. The hemoglobin was 11.5 Gm. and the red blood count was 3,900,000 cells per cubic millimeter. The blood urea nitrogen was 12 mg. per cent, the glucose 97 mg. per cent, and the carbon dioxide combining power 34 volumes per cent. A urinalysis revealed a specific gravity of 1.016, a pH of 4, 1 plus proteinuria, 2 plus glycosuria, 1 plus acetonuria, 3 to 5 white blood cells per high-power field, a rare red blood cell, and no casts.

During the first day the patient became somewhat dehydrated with fever and a dry warm skin. Her blood pressure remained about 80/40. She coughed a few times and raised a little clear mucus. This did not reveal any unusual cellular elements. She received some sedation with chloral hydrate. On the second day the temperature had become normal and it remained essentially so throughout the remainder of her period of hospitalization. The cardiac rate on the second day was 110 per minute and the respirations were 38 per minute. She raised a very small amount of white sputum.

A chest x-ray (Fig. 2), taken 30 hours after the first one, shows a moderate general decrease in the character and extent of the widely distributed densities. The clearing is most evident in the left lung and the basal portion of the right lung. There are no signs of effusion.

On the second day the electrocardiogram showed some flattening of the T waves in the precordial leads.

Physical examination revealed diminished breath sounds and dullness to percussion at both bases. These findings were more pronounced on the right side. There were no pulmonary râles of any type, nor did any râles appear at any time during her period of illness. The blood pressure had fallen to 74/10 on the third day of her illness and she still required oxygen by nasal catheter but this was reduced to 8 L. per minute. She raised one specimen of bloody sputum. The prothrombin activity was 90 per cent of normal.

Bleeding time was 1 minute and clotting time 10½ minutes. There was normal clot retraction at 24 hours. The white blood count was 17,700 with 84 per cent polymorphonuclear leucocytes, 15 per cent lymphocytes, and 1 per cent monocytes. Oxygen therapy was continued for five days before she could breathe comfortably without it.

A chest x-ray taken on the sixth day (Fig. 3) shows in comparison to the previous films further clearing of the densities. There is no parenchymal infiltration and only a minimal increased prominence of the pulmonary markings in the lower half of both lung fields. The mediastinum shows no widening. The heart shadow has normal contours. The transverse diameter measures 13 cm. The intrathoracic diameter measures 27.8 cm.

An electrocardiogram showed that the precordial T waves had returned to normal.

Her condition gradually improved but it was not until the seventh day that the respirations slowed to a more normal rate of 22 and the pulse to a rate of 84. On the ninth day the physical examination revealed the lungs clear except for a small area of diminished breath sounds at the right base laterally. On this day the white blood count was 13,000 cells per cubic millimeter with 76 per cent polymorphonuclear leucocytes, 19 per cent lymphocytes, 4 per cent monocytes, and 1 per cent eosinophiles. There were 9.5 Gm. of hemoglobin and the red blood count was 3 million cells per cubic millimeter.

On the eleventh hospital day the patient was well enough to sit up and was discharged to continue convalescence at home. A pelvic examination prior to discharge revealed a deep tear in the anterior lip of the cervix extending into the anterior fornix.

Following discharge the mother and baby have been well. Repeat chest x-rays and electrocardiograms have been normal. The mother's anemia responded well to iron therapy and no transfusion was needed.

Summary and Conclusions

Thirty-five fatal cases and one nonfatal case of maternal pulmonary embolism by amniotic fluid have been previously reported in the literature. A nonfatal case occurring in a primipara is reported. It is suggested that further nonfatal cases could be detected by immediate postdelivery chest x-rays, and electrocardiographic studies.

Oxygen in adequate amounts together with aminophylline and other supportive measures is the most effective therapy for treating the acute episode.

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203 THAYER STREET

CARCINOID OF THE APPENDIX*†

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SOME gynecologists remove the appendix as a prophylactic measure at the time of pelvic surgery. Others, however, condemn this procedure as causing an increased morbidity, since the appendectomy converts a clean case into one that is potentially infected. In a recent report from the Mayo Clinic by Pratt, Lee, Hasskarl, and Brandes[1] this possibility was investigated. A prophylactic appendectomy was done in approximately one-half of 373 patients undergoing abdominal hysterectomies. It caused no increase in morbidity.

Two other recent articles have called attention to the surprising incidence of acute inflammation in routinely removed appendices. Rosset and Conston[2] found acute inflammatory changes in 12 per cent of 210 appendices. Taniguchi and Kilkenny[3] report an incidence of 10.5 per cent in 532 such specimens. These authors urge a continuance of prophylactic appendectomy because of these findings.

At Wesley Memorial Hospital, prophylactic appendectomy is done almost routinely, providing the patient is in good condition and the appendectomy is not unusually complicated. One such appendix, grossly normal, was found on pathologic examination to contain a "carcinoid" tumor.

General reviews on "carcinoids" by Pearson and Fitzgerald[4] and by Willis[5] have dealt with these tumors in detail. Although they may arise elsewhere in the gastrointestinal tract, the overwhelming majority are appendical in origin. This tumor arises from cells found normally in the gastrointestinal tract that have been given a variety of irrelevant names. These cells contain cytoplasmic granules that are stained specifically by silver salts. Since the tumor cells also retain the property and since the tumor is malignant, the term *argentaffin carcinoma* is preferable to "carcinoid." The tumor grows and metastasizes slowly. When primary in the appendix, it spreads even more slowly than when originating in other areas. Even so, it is a definite carcinoma, and if given time will kill the patient.

The patient was a 28-year-old Negro woman with a preoperative diagnosis of multiple uterine myomas. The diagnosis was confirmed at operation, and a total abdominal hysterectomy and prophylactic appendectomy were done. The pathologic diagnosis was uterine myomas, adenomyosis, endometriosis of the serosa of the appendix, focal subacute inflammation of the appendix, and carcinoid tumor of the appendix. The postoperative course of the patient was uncomplicated.

The intact appendix was grossly normal and the lumen patent except for a portion near the tip about 1 cm. in length. Here it was obstructed by a firm, grayish-yellow tumor.

In the region of the tumor (Fig. 1), the lumen was either small and displaced to one side or entirely replaced by islands and cords of epithelium-like cells interspersed in a lacework of moderately heavy connective tissue. These cells were round or polyhedral in shape, with a small amount of eosinophilic cytoplasm, an oval or round vesicular nuclei containing one or occasionally two large nucleoli. There was no definite acinar arrangement of these cells. No mitotic figures were seen, nor was there noteworthy variance in the size of cells or in the size, shape, or staining qualities of nuclei. The tumor was principally submucosal in position, but extended into, although not completely through, the outer muscular layer of the wall. With Masson's argentaffin stain[6] (counterstained with hematoxylin and eosin) the cells contained intracytoplasmic argentaffin granules typical of such tumors (Fig. 2).
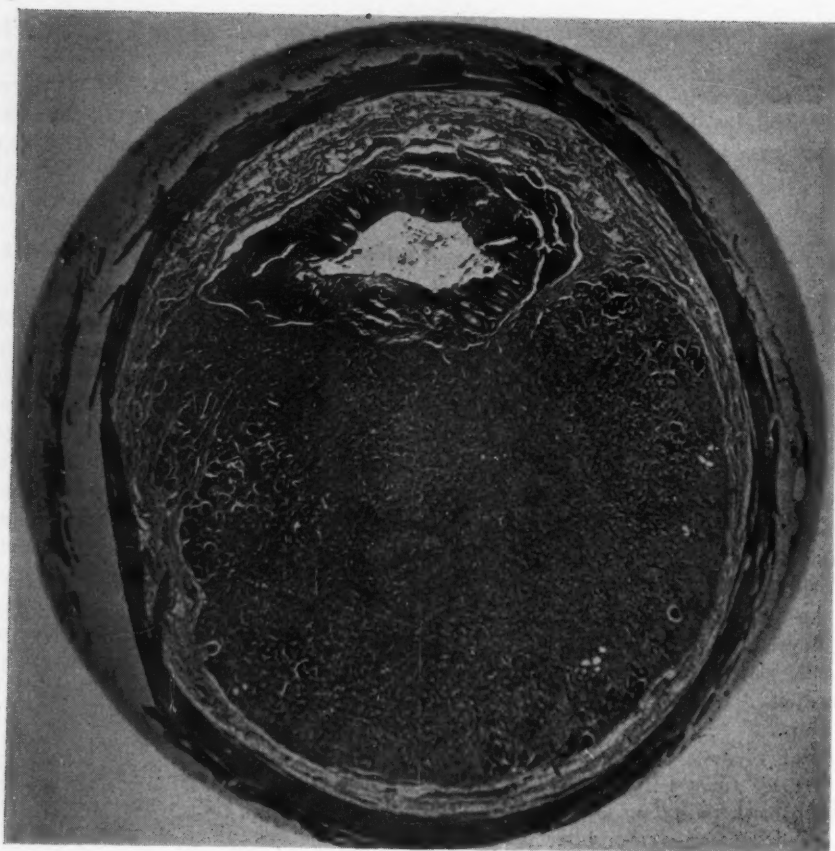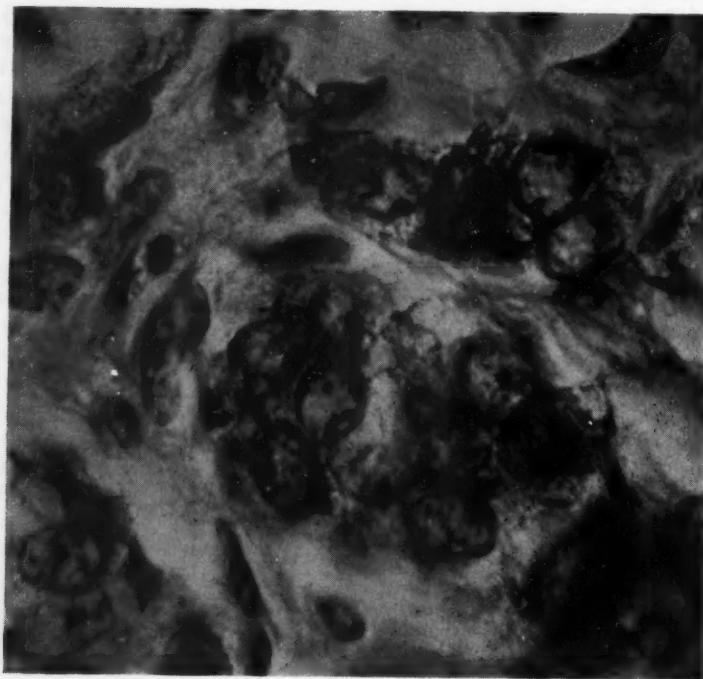
Fig. 1.

Fig. 2.

Comment.—This patient was in her third decade which is the time such tumors of the appendix are most frequently discovered. No gross evidence of the lesion or of metastases was apparent. Of course, this lesion was not suspected preoperatively.

Even though "carcinoids" of the appendix grow slowly, and usually do not metastasize until the fifth decade or later, they may eventually cause death by their metastatic growth. It is therefore felt that this patient has been rendered a disinct service through the incidental removal of her appendix.

We are in wholehearted agreement with those who advocate routine appendectomy at the time of pelvic surgery, and offer this case as an added example of the value of this procedure.

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ABDOMINAL PREGNANCY TERMINATING IN A LIVING CHILD AND COMPLETE REMOVAL OF PLACENTA

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THIS case is reported because of the unusual pathologic relationship between fetus and mother, the patient's interesting history and symptoms, and to add to the available literature on abdominal pregnancy with delivery of a living child and complete removal of the placenta.

Case 60791, G. G., aged 31 years, Negro, missed her first period July, 1950. She gives a history of a questionable pregnancy of two months' duration some years ago which terminated in an abortion. There is also a history of an appendectomy in 1937, the appendix was ruptured, requiring drainage and a hospital stay of two weeks after operation. About Aug. 12, 1950, the patient had a gastric upset with vomiting, nausea, intestinal cramps and diarrhea and went to a private physician who diagnosed her condition as being due to food poisoning. The physician at this time found no clinical evidence of pregnancy and the patient continued to have gastric distention, soreness, and abdominal pain with alternate attacks of loose stools and sought the advice of another physician who gave her no relief and failed to make the diagnosis of pregnancy. After three months of abdominal distress she visited another local physician who made a diagnosis of tumor of the uterus and gaseous distention; during this interval patient had no vaginal bleeding and her complaints were: (1) she thought she was pregnant but could get no confirmation from various physicians, (2) abdominal distention, pains in "bottom of stomach," cramping, and dark stools.

Around the fifth month the patient felt what she thought was "fetal movement" and went to another physician who told her she was pregnant and that the distention was due to the fact that the baby did not have enough room in the upper abdomen. She continued to visit this doctor and in the sixth month, following a task of scrubbing and mopping, the patient noted a vaginal bloody discharge with pain in the lower abdomen and called her physician who told her she was threatening to abort, advised her to stay in bed, and gave her conservative treatment with subsequent subsiding of symptoms. During the seventh month she made another visit to the physician complaining of hemorrhoids which were treated satisfactorily. After seven and one-half months of pregnancy the patient developed a persistent diarrhea with intestinal cramps, gaseous distention, and nausea from which three weeks of continous treatment by her doctor failed to give her relief and resulted in her coming to me on Feb. 26, 1951. Note: Prior to this time no one had made a statement relative to a "suspicious abdominal pregnancy." When the patient was seen by me she gave the above history and it was quite evident that she was 7 to 8 months pregnant. During her wait in the office she passed several diarrheal stools; she was treated for the diarrheal symptoms and told to return in two days. On her return it was noted that patient was decidedly edematous, her blood pressure was 190/110, albumin 4 plus, her eye grounds indicated vascular hemorrhage, and the impression was that the patient was in a severely pre-eclamptic condition. Hospitalization was advised with a view toward a clinical and pathologic evaluation of her condition and a decision as to how best to manage this case.

The patient entered the hospital on March 5, 1951, and the following laboratory data were received:

March 5, 1951: Urinalysis: color, dark amber; reaction 5.0; specific gravity 1.032; albumin 4+; sugar, none. Microscopic examination: packed with hyaline casts 4+; granular casts 2+; epithelial cells 4+.

March 6: White blood count 9,000; red blood count 4,050,000; hemoglobin 10.1 Gm. per cent; nonprotein nitrogen 22 mg. per cent; blood sugar 76 mg. per cent; total proteins 6.6 Gm. per cent; albumin 2.6 Gm. per cent; globulin 4.0 Gm. per cent.

March 15: Urinalysis (catheterized specimen): color, yellow; reaction 5.5; specific gravity 1.015; albumin 2+. Microscopic examination: leukocytes 2+; epithelial cells 2+; *Trichomonas vaginalis* 2+.

March 16: Nonprotein nitrogen 36 mg. per cent.

X-ray Report, March 6, 1951: Examination of the abdomen revealed a single fetus of approximately eight months' gestation in transverse position. The arms were caudal and presenting; the back was cephalad. The head lay anteriorly in the iliac region. The fetal skull appeared somewhat flattened.

Impression: Single pregnancy, transverse.

It was decided that since the patient was a fairly elderly multipara whose only other pregnancy resulted in a questionable abortion at 2 months and who was very desirous of a viable child and who presented all the physical symptoms and clinical signs of eclampsia with x-ray findings of a definite 8 months' gestation, the best procedure was to do a cesarean section after getting the patient in the best physiologic condition possible.

Operation.—On March 7, 1951, under spinal anesthesia, the abdomen was opened through a long left paramedian incision revealing a thickened amnioticlike sac occupying the upper part of the abdominal cavity containing a viable male fetus weighing 5 pounds, 6 ounces with talipes calcaneous, right. The infant cried lustily when delivered and required no resuscitation. The placenta was found attached to the posterior right lateral portion of a large mixed-fibroid uterus and to the right tube, right ovary, and right broad ligament, and there was another attachment to the terminal portion of the ileum and mesentery; the placenta was apparently receiving at this time most of its blood supply from the vascular uterine myoma and the adnexa on the right side. The placenta was freed from the ileum and its mesentery, leaving a small portion of its capsule attached at this site and a Porro operation was done supracervically, delivering the placenta in toto, attached to the uterine fibroid and its surrounding adnexa; bleeding was controlled; the cervical stump peritonized and the abdomen closed without drainage. The patient's condition during the operation was normal; 500 c.c. of blood were started and given during the procedure.

Pathologic Examination.—The specimen consisted of a supracervically amputated uterus, both tubes, ovaries, and attached extrauterine placenta. The uterus measured 7 by 8 by 10 cm. It was symmetrical and showed a smooth serosa except at the site of placental attachment. A leiomyoma measuring 6 by 4 by 4 cm. was attached to the serosal surface by a narrow pedicle. On opening the uterus, three smaller tumors of similar nature were found within the endometrium. The endometrium was symmetrical, 4 mm. in thickness, gray white in color, and spongy in consistency. The placenta was kidney-bean shaped and measured 20 by 15 by 3 cm. Except for its attachment, it was completely covered by its membranes. One area of thickening within the membranous sac which was adherent to the intestine was found to be a separate mass of placental tissue measuring 5 by 4 by 2 cm. The placental mass proper was attached firmly to the right lateroposterior surface of the uterus and to the right tube and broad ligament. This attachment covered an area of approximately 36 sq. cm. The area contained vascular channels measuring up to 2 mm. in diameter, derived from the vessels of the myometrium and the broad ligament. Both tubes showed evidence of old inflammatory change in their thickened, fibrosed walls. The right tube was adherent to the placental attachment and it could not be ascertained grossly whether the original implantation was within this tube. Despite the thickened wall and adhesions the right tube had a free fimbriated end. The opposite tube was similar. It measured 6 cm. in length and up to 1.3 cm. in diameter. Areas of cystic dilation occurred throughout the lumen. The fimbriated end was fused and completely closed. The ovaries each measured 2 by 1.5 by 1.5 cm. They had smooth serosal surfaces and on cut section each contained numerous peripheral simple cysts measuring up to 4 mm. in diameter. A large corpus luteum was found in the right ovary measuring 5 mm. in diameter.

Microscopic Examination.—The myometrial tumors showed the characteristic appearance of leiomyomas with little evidence of hormonal stimulation. One tumor was almost completely hyalinized. The large vessels coursing through the myometrial wall to the placental attachment were hypertrophic. The uterine serosa in this area showed a decidual reaction. Large pale decidual cells were also found in the stroma of the right ovary and extensive decidual reaction was seen in the mucosa of both tubes. It was interesting to note that the decidual cells universally replacing the tubular mucosa appeared better differentiated than those found in the endometrium proper. The right tube showed evidence of old inflammatory disease indicated by fusion of mucosal villi to form dilated cystic luminal spaces. The walls of both tubes were fibrosed and contained scattered mononuclear inflammatory cells. The uterine part of the right tube appears to be patent in the sections made. The right ovary contained the corpus luteum of pregnancy as well as the serosal decidual reaction noted. Some serosal surfaces in the right parametrium were infiltrated with polynuclear and mononuclear inflammatory cells. The endometrium was composed of a thick layer of decidual cells which were undergoing extensive degenerative changes. The placenta contained well-vascularized chorionic villi but large areas of hyaline necrosis were seen throughout. In the area of uterine attachment islands of syncytial cells still remained.

The mother had an uneventful recovery and both mother and infant left the hospital on the thirteenth postnatal day. The infant was placed under the care of an orthopedist and a cast was applied to the right foot for correction of the talipes. There was some concern as to the mentality of the child, from his facial appearance at birth but seven months later the infant is a normal, healthy, alert child weighing 15 pounds, 14 ounces.

LIPOMA OF THE UTERUS

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LIPOMAS of the uterus are rare. In 1857 a drawing by Lebert[1] in a pathological atlas was labeled as representing adipose tissue in the uterus. This appears to be the first recorded case. Since that time there have been sporadic reports in the literature, mostly from Europe at the turn of this century. In 1903 Seydel[2] reviewed the literature and found 10 cases of fatty tumors of the uterus. Three other cases he felt should not be included because they were not studied histologically. In 1917 a case was presented by Elkin and Haythorn[3] as well as three more quoted from the literature. Peterson[4] in 1922, in an exhaustive review of mixed tumors of the uterus, found 31 fatty tumors, including all of the above cases. Only 10 of these he felt were pure lipomas. In a more recent review by Ritter and Stringer[5] 13 cases were added from the literature as well as one of their own. At least two of these would appear to be fatty degeneration of fibromyomas. Since that time two more cases have been presented in the literature and one of these (Peake's[6]) appears to be a degenerated fibromyoma. Since 1857 there are, therefore, 23 lipomas of the uterus reported in the literature.

L. L. (8435-51), a 50-year-old Negro woman, was admitted to Bellevue Hospital Feb. 26, 1951, because of descensus of the uterus. The past history was not significant except that the patient had had two spontaneous abortions 28 years before, followed by a normal delivery of a term child by a midwife. The patient had an uneventful menopause in 1947. She had never had a surgical operation.

Significant physical findings were confined to the pelvis. There was a complete prolapse of the uterus, which was felt to be normal in size. There were a small cystocele and rectocele.

Operation.—A vaginal hysterectomy, anterior colporrhaphy, and perineorrhaphy were performed.

Macroscopic Examination.—The corpus measured 5 by 4 by 2.5 cm. and was smooth and regular in outline except for an area near the right cornu where the serosa showed slight bulging. This was softer in consistency than the surrounding tissue. On section of the corpus this was revealed to be a well-circumscribed intramural mass 3½ cm. in diameter of the typical yellow color and greasy consistency of fatty tissue. Its cut surface bulged slightly over the surrounding myometrium. Further sectioning of the corpus disclosed a solitary intramural fibromyoma 1 cm. in diameter on the left anterior wall of the corpus. The endometrium was thin and uniform and the cervix was elongated to 5.5 cm. in length and showed stenosis of the cervical canal in its midportion.

Microscopic Examination (Fig. 1).—Microscopic study of the corpus showed a myometrial pattern of atrophic muscle bundles with numerous intervening thick-walled, sclerotic blood vessels. Scattered through the myometrium were a few small atrophic endometrial glands with sparse stroma. Completely surrounded by myometrium was a sharply delineated area of adipose tissue made up of typical fat cells with abundant clear cytoplasm and a flattened eccentric nucleus. The uniform pattern of these cells is interrupted only by small septa of connective tissue in which are seen small thin-walled blood vessels. There were no fibrous or muscle elements in the tumor. Sections of this tissue stained by sudan III shows abundant red-staining fat. In the myometrium fine droplets of fat are detected adjacent

to the lipoma but this is attributed to dispersion of fat on sectioning the tissue. No intracellular fat can be detected in the muscle cells or in the connective tissue.

Section of the cervix showed a chronic inflammatory reaction with areas of epidermization.

Comment.—Clinically lipomas of the uterus are of little significance. Most tumors recorded are found in postmenopausal women. Probably the youngest was the case of Reich and Nechtow[7] in a patient 39 years old. The interest rests in their origin. Robert Meyer, discussing Seydel's paper, pointed out that there is no fat found in the normal uterus except that which he has demonstrated extending from the parametria into the uterus along with and surrounding blood vessels. This fat is never seen to any great extent. If this does not represent the origin of the tumors, their explanation becomes somewhat more complex. Knox[8] felt these tumors arose from embryonic cell rests. Elkin and Haythorn point out that if Meyer's views are correct, and there is no fat in the uterus, the theory of cell rests can be excluded, as there would be no anlage for fatty tissue in an organ which contains no fat. Merkel[9] postulated that these tumors as well as mixed tumors of the uterus had their origin in displaced embryonal rests along the Wolffian duct.
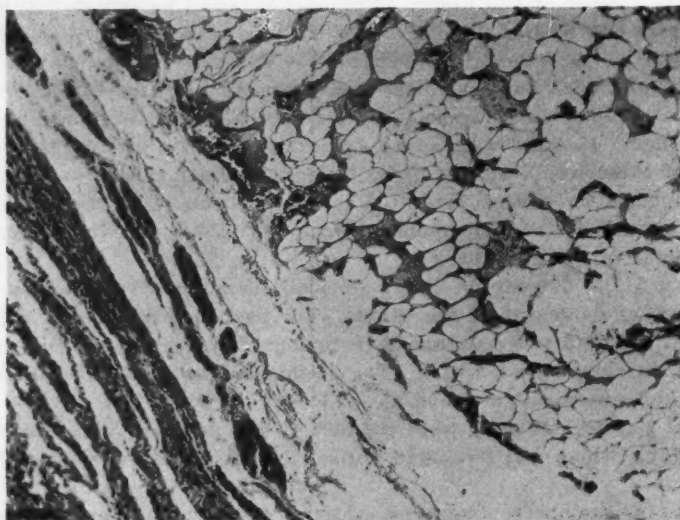

Fig. 1.—Lipoma of the uterus, showing typical adipose tissue cells.

This is in accordance with the Wolffian duct theory of Wilms. These authors also exclude the possibility of the tumors arising from fat surrounding blood vessels because of the constant findings of vessels in the connective tissue bundles of the tumors and not in the fatty areas. Elkin and Haythorn were able to draw very interesting conclusions from study of their case. They assumed that since highly specialized cells such as heart-muscle cells, striped-muscle cells, liver, adrenal, and glandular epithelium were able to take up fat in a globular form, it should be possible for connective tissue, which is much less specialized, to do so as well. They were able to offer some support for this when they identified smooth-muscle cells in their specimen by demonstrating their fibrils. None of the cells so identified was found to contain fat in a granular or globular form. They therefore concluded that the tumor arose either from lipoblasts or connective tissue. They were then able to demonstrate fibroglia in the connective tissue but were unable to find them in the fat cells. They believe, therefore, that their tumor had its origin in lipoblasts displaced during early development. This is a theory earlier advanced by Seydel.

Brunnings,[10] in reporting an early case, ascribed the tumor to metaplasia of fat cells from muscle cells, a view held also by Lockyer[11] and Von Franqué.[12] The only other author

who lends support to this theory is Peake, who felt he was able to show a gradual change of smooth-muscle cells into alveolar fat. It would seem that this more probably represents fatty degeneration of muscle cells, rather than true metaplasia.

Starry,[13] studying another tumor, was able to demonstrate small amounts of fat in the connective tissue. He could not demonstrate fat in muscle cells. He believes that the tumor had its origin in connective tissue, possibly a specially differentiated lipogenic type.

A case has been recorded by Pollack,[14] who feels that the tumor was probably due to omental fat which was caught in a wound of the uterus at a previous operation.

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CARCINOMA OF THE MESONEPHRIC DUCT*

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VESTIGIAL remnants of male structures not infrequently exist in the female pelvis. That histopathological changes may produce neoplasms of these remnants, as manifest by the fairly common appearance of parovarian cysts and Gartner duct cysts, is also well established.

One factor, however, that is commonly overlooked is that the mesonephros, embryologically, is a structure of considerable length in the female fetal pelvis. During the course of its development and degeneration, portions of the mesonephros may remain near the ovary, in the mesosalpinx and in the broad ligament. In its caudal relationship, the mesonephros becomes a duct structure, the so-called Wolffian or mesonephric duct. And as such it lies in the lateral cervix, anterior lateral cervix, or in the anterior lateral vaginal wall.

This paper is confined to neoplastic changes of remnants of the cervical portion of the mesonephric duct.

Huffman,[1] in 1948 studied 1,192 surgically excised cervices and found evidence of mesonephric remnants in ten of his specimens. Five of these were neoplastic and one was an adenocarcinoma. In his very excellent paper, Huffman reviewed the literature on this subject and discussed the embryological, histological, and pathological aspects of this problem.

Three types of neoplastic changes may occur in mesonephric cervical remnants, these being cystic changes, adenomas, and adenocarcinomas.

Fifteen papers have appeared on this subject dating from 1897 to 1948. Robert Meyer[2] first described the adenomatous change in 1897, and the adenocarcinoma variety in 1903.[3] Henkel[4] reported cystic examples in 1920.

Previous to Huffman's paper in 1948, the American literature contains one other reference to this subject; that of Wolfes[5] in 1940.

Six adenocarcinomas of the mesonephric duct now appear in the literature and the case report to follow represents an as-yet-unreported seventh example.

Case Report

This 47-year-old white woman, nulliparous, a school teacher, was referred to me by her family physician Sept. 25, 1948.

Approximately two years before I saw her, she noticed what she described as a feeling of moisture in the vaginal region. This she attributed to the recurrence of a childhood "kidney condition." Because of its persistence however, she consulted her physician who assured her that the problem was not of renal origin but, instead, was due to a *Trichomonas vaginalis* vaginitis.

The treatment consisted of multiple vaginal insufflations and vinegar douches. After about a year of this type of therapy without the relief of the symptoms, she was referred to a general surgeon, who hospitalized her for further study and did a cervical biopsy, dilatation and curettage, all of which were negative for malignancy and revealed a chronic cervicitis and a normal endometrium.

Shortly before she was referred to me she noticed for the first time that, following douching or intercourse, the discharge became blood tinged. This latter symptom prompted her physician to seek further help and, after taking a Papanicolaou smear, which was negative, he sent her to me.

At her initial examination the external genitals were negative except for the appearance of a thin watery discharge bathing the introitus. The Skene and Bartholin glands were normal. In the region of the right fornix was a granuloma-like lesion. The cervix was

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separated from this lesion by about 0.5 cm. of normal vaginal mucosa and except, for a superficial erosion, appeared normal. There was a thickening of the right perimetrium to both vaginal and rectovaginal examination. The uterine fundus was normal as were both adnexa.

A tentative diagnosis at this time was a chronic granuloma with what seemed to be a possible sinus tract extending into the right broad ligament. The etiology was questionable, but granuloma inguinale, lymphopathia venereum, chancroid, or syphilitic or tuberculous lesions were considered. Also noted in the differential diagnosis was primary vaginal carcinoma or metastatic carcinoma from the cervix, endometrium, or even the adnexa. Remotely considered were such lesions as ureterovaginal fistula, or a foreign body left from an appendectomy 15 years previously.

A diagnostic study was then undertaken which revealed a normal red blood count and sedimentation rate, a negative urinalysis, a negative serology and dark-field examination, and a negative Frei test. Smears and cultures of the discharge revealed normal vaginal flora and no Trichomonads, mold, or yeast. There were no Ducrey's bacilli found, no Donovan bodies, and Papanicolaou smear showed no malignant cells. The Mantoux test was negative, and the chest x-rays were normal. Intravenous urogram and abdominal flat plate were normal and I even gave the patient methylene blue by mouth and had her insert vaginal tampons hoping possibly to demonstrate an unrecognized renal-tract fistula. The tampons remained unstained.

At about this stage in the examination the patient was hospitalized and examined under anesthesia and nothing more was found than originally had been discovered, except that the lesions seemed definitly to be separate from the cervix or fundus. Smears and cultures were again repeated. Guinea-pig inoculation was done, the endometrium was re-curetted, and biopsies were taken of the cervix and the granuloma. Lipiodol was instilled in both the uterus and in the sinus tract, and x-ray revealed no communication between these two areas. Except for chronic inflammatory tissue reported from the cervical biopsy and vaginal lesion, all the tests were negative.

Being unable to establish the etiology of the lesion, I referred the patient to Dr. Stearns at the University of Oregon Medical School, who also repeated the Papanicolaou smear and found it to be negative. Dr. Stearn's report stated, ''When I examined her my fingertips said carcinoma immediately, for the cervix seemed thick, obscure and the lesion involved most of the anterior fornix and was creeping definitely forward on to the bladder wall, or rather perhaps the anterior vaginal wall. Her prolonged history without pain or loss of weight certainly would refute carcinoma, as does also your biopsy and the Papanicolaou smears. But I cannot conceive of any other lesion that would produce such fixation, such a tendency to bleed on touching and frankly I would be inclined to treat her as a carcinoma by radium irradiation, followed by deep x-ray therapy. At the time the radium is applied, I certainly would be inclined to take other biopsies of various areas, making them reasonably deep, for it is possible that this is an extremely indurating type.''

On Jan. 31, 1949, or fifteen months after I first saw her and in excess of three years from the onset of her symptoms, the patient was readmitted for operation with the preoperative diagnosis of carcinoma of the cervix, invasive type, or possibly carcinoma of the right mesonephric duct. (This latter diagnosis had been prompted by Dr. Huffman's paper in this JOURNAL.[1])

Surgery was preceded by cystoscopy to rule out a possible bladder neoplasm in spite of negative urinary-tract symptoms. The cystoscopy was negative. This time I first curetted the endometrium, then curetted and took a cervical biopsy. Frozen sections of these tissues were again negative. Then the lesion in the vaginal fornix was dissected. At a level of about 2.5 cm., a bit of friable, pulpy tissue was found and a generous portion of this tissue was removed. Frozen section of this tissue revealed adenocarcinoma. Still not satisfied as to its origin, I did a laparotomy and discovered the lesion to be occupying the entire right base of the broad ligament infiltrating the lateral pelvic wall. Although it was involved by invasion, the cervix and uterine fundus were separate from the neoplasm to gross examination.

Because it was felt that the lesion was not operable, the patient was referred to the radiologist immediately postoperatively with the diagnosis of adenocarcinoma of the mesonephric duct.

She received 4,000 r delivered through two portals followed by 2,200 more, six months later. Because of the lateral ramifications and since it was not primarily a cervical lesion, radium therapy was not employed. There was a rapid degeneration of the patient's condition by this time as manifested by the occurrence of pain, particularly intractable in nature, referred to the right leg, loss of weight, and repeated exsanguinating vaginal hemorrhages. She became febrile two days before her death and appeared quite toxic, finally developing a deep icterus which persisted until death on April 3, 1950.

Autopsy examination revealed the immediate cause of death to be infectious hepatitis secondary to right renal and perirenal abscess. There was adenocarcinoma involving the entire right pelvis with occlusion of the right ureter. Adenocarcinoma had also involved the bladder wall and was found in the preaortic lymph nodes. Microscopic examination revealed the lesion to be a highly anaplastic variety of adenocarcinoma. Serial sections of the cervix demonstrated that this structure had been almost entirely obliterated by fibrous tissue with occlusion of the endocervical canal. Adenocarcinoma involved the serosal and lateral myometrial layers of the uterus. The gross description of the vaginal lesion was as follows:

"The vaginal canal is surrounded by scar tissue which extends into the right adnexa. The right fornix is enlarged having dissected into the right broad ligament for a distance of 3 to 4 centimeters. Here the wall is rather markedly hemorrhagic and this apparently represents the focus of bleeding noted clinically. There is no opening from the endometrium into the vagina, and the cervical os was obscured in scar tissue. The scarring extends into the right pelvic brim and right renal fossa. There is an irregularly shaped sinus in the form of an abscess whch has involved and occluded the ureter by dense scar tissue. The right kidney has been replaced by an abscess cavity."

The pathologist, Dr. Charles Larson, felt that the adenocarcinoma in the right perimetrium was consistent with that of an adenocarcinoma of the mesonephric duct. His comment was, "The location of the material from biopsy, the repeated absence of malignancy in the uterine curettings and cervical biopsies strongly suggest a dysontogenetic origin for this tumor, the most likely source being the Wolffian or mesonephric duct remnants which run lateral to the uterus and upper vagina and are present in the broad ligament."

Summary

That mesonephric remnants may persist in the adult lateral cervix is an established fact. That, in turn, these embryological structures may undergo malignant change is not generally appreciated.

Since routine examination of cervices histologically may be limited to sections that do not include the lateral cervix, perhaps many of these remnant structures are overlooked.

Gainey, in his discussion of Huffman's paper, postulates that perhaps certain cervical adenocarcinomas have their origin as mesonephric duct carcinomas. Certainly, as this paper illustrates, unless the diagnosis of mesonephric-duct adenocarcinoma is entertained in lesions not typically cervical in origin, a magnitude of confusion exists in the gynecologist's mind as he seeks a diagnosis. Too much time may be consumed before the diagnosis finally is achieved, time that can be ill afforded by the doctor or his patient, if prognosis for recovery with proper therapy is to be anything but dismal.

A seventh case of mesonephric-duct carcinoma, which diagnosis seems to meet the necessary criteria for establishing such an entity, is presented.

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1312 MEDICAL ARTS BUILDING

MULTIPLE SCLEROSIS COMPLICATING PREGNANCY

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MULTIPLE sclerosis has been a well-known disease entity for many years, but, in the American literature at least, not much has been written concerning the effect, if any, it exerts upon the course of pregnancy. In 1945 Peckham[1] reported two cases and in his very thorough review of the literature concluded that no indictment of the disease could as yet be made because of an insufficient number of reported cases here in the United States. Birner[2] and Kushner[3] each reported one case in which an apparent improvement occurred in the disease following delivery. Douglas and Jorgensen[4] reported five cases and concluded that multiple sclerosis has no ill effect upon the course of pregnancy or upon the offspring. They also felt it to be no indication for therapeutic abortion. Edwards and Edwards[5] reported one case of advanced multiple sclerosis complicating pregnancy in a 42-year-old multigravida who was successfully delivered at term by cesarean section. No ill effect was noted on the course of the disease nor the pregnancy. Hawn[6] reported two cases of postpartum optic neuritis in patients with multiple sclerosis. He feels that the disase is definitely made worse during pregnancy and in cases where there is a gross disturbance of physical and psychic capacity the pregnancy should be interrupted and a sterilization operation performed. The following case is reported in detail because of the grave obstetrical problem that arose during the last few weeks of gestation further complicating the clinical picture. The pathology involved, besides being of definite value for teaching purposes, was considered to be of extreme interest to anyone engaged in the practice of obstetrics.

Case Report.—D. P., a 30-year-old, white, gravida iii, para ii, dependent wife who was known to have had multiple sclerosis since 1948, presented herself to the hospital admission unit on the evening of Aug. 4, 1949, with the complaint of vaginal bleeding for the previous four hours. Her last acute exacerbation of the multiple sclerosis had occurred two months prior to this admission. Her last menstrual period was given as Jan. 10, 1949, and the expected date of confinement was calculated to be Oct. 17, 1949. The prenatal course had been uneventful to date with the exception of the exacerbations of the multiple sclerosis. Physical examination revealed a uterine enlargement to the size of a pregnancy of seven calendar months. The fetal heart tones were audible in the left lower quadrant and the only other positive findings were a lateral nystagmus bilaterally, right-sided muscular weakness, and weak abdominal reflexes. Following typing and cross-matching a vaginal examination was made to determine the source of the bleeding. The cervix was badly eroded and bled easily on contact. The vertex was presenting and the cervix was 50 per cent effaced and would admit only two fingers. No placenta could be felt near the internal os. The impression was that of bleeding from a cervical erosion with no evidence of placenta previa. The patient was placed on bed rest for 24 hours and then permitted to get up prior to being discharged. However, upon getting out of bed she immediately lost her equilibrium and fell to the floor. Examination revealed a marked slurring of speech, extreme muscular weakness on the entire right side, and diplopia. Medical consultation was obtained and measures initiated to treat the multiple sclerosis. Priscol in doses of 25 mg. three times a day was given without much success. After nine days of conservative treatment the symptoms abated and the patient was

discharged to her home for the remainder of her prenatal course. The date of discharge was Aug. 29, 1949. No more trouble was encountered during the remaining weeks until she again presented herself to the hospital on Oct. 4, 1949, at about 38 weeks' gestation with the complaints of vaginal bleeding for one day and cough and chest pain for about one week. Examination at this time revealed an apparently full-term pregnancy with audible fetal heart tones in the left lower quadrant. The neurological findings were as previously noted. It was deemed advisable to give the patient 500 c.c. of whole blood and perform another vaginal examination. During the examination the examiner inadvertently started profuse bleeding from the uterus with the cervix only 3 cm. dilated and 50 per cent effaced. The vertex was still presenting and it was decided to attempt tamponade of the low-lying placenta with scalp traction and thereby control the bleeding. This was accomplished with considerable difficulty and bleeding was apparently controlled. The fetal heart could still be heard in the left lower quadrant. Blood replacement was energetically continued and the patient was watched very carefully for any evidence of renewed hemorrhage. After about five hours of apparently satisfactory labor it was noted that the uterus was not relaxing as well between contractions and the fetal heart could no longer be heard. In view of the signs of continued intrauterine hemorrhage and despite the possibility of a dead baby it was decided to deliver the patient by cesarean section in order to control the bleeding better from the placental site after emptying the uterus. The patient had received to this time 1,500 c.c. of whole blood and another 500 c.c. transfusion was started. Under 8 mg. of Pontocaine spinal anesthesia the abdomen was opened in the lower midline and the lower uterine segment was exposed by reflection of the bladder peritoneum. The entire uterus was noted to have a dusky purplish hue. The lower uterine segment was incised vertically and profuse bleeding was immediately encountered from the underlying placenta and large maternal venous sinuses. The infant was rapidly delivered from left occipitotransverse position and was noted to be alive. The placenta was removed manually with some difficulty due to its being partially adherent to the uterine wall. Severe and profuse bleeding continued from the placental bed and no amount of oxytocics would produce any sustained contraction of the uterus. An attempt was made to suture the bleeding sinuses but the sutures cut through and caused more bleeding. In order to control the hemorrhage it was decided to remove the uterus. A subtotal hysterectomy was done without incident and all bleeding points were ligated with chromic No. 2 suture material. The abdominal wound was closed with chromic No. 2 in the fascia and clips were placed in the skin. A total of 1,000 c.c. of whole blood was given during surgery. The patient was sent back to the ward in good condition. The infant had responded to resuscitation and had been sent to the nursery for the newborn in apparently good condition. The mother was given 100,000 units of aqueous penicillin every three hours and all the usual postoperative precautions were carried out. Another 1,000 c.c. of blood were given during the postoperative course and the skin clips were removed on the seventh postoperative day revealing a well-healed abdominal wound. The appearance of a right-sided headache plus blurring of the left visual fields bilaterally was the only flare-up of the multiple sclerosis during her stay in the hospital and this occurred for only a few hours on the tenth postoperative day. The patient was discharged home with her baby on the eleventh postoperative day in apparently good condition. At her six weeks postnatal check-up the cervical erosion was cauterized with the electrocautery and daily douches were advised until her next visit in six more weeks. Upon her return to the clinic she claimed to be feeling well and had noted no return of her disease. The cervix was well healed and the remainder of the pelvic examination revealed no active pelvic pathology. However, on March 10, 1950, the patient was again admitted on the medical service for treatment of another exacerbation of the multiple sclerosis and after about one week was sent home with symptoms having subsided. At the present writing I am unable to state the whereabouts or the state of health of this patient as I am no longer in the section of the country in which she resides.

Pathologic Report.—The specimen consisted of a supracervically amputated post-partum uterus weighing 3,000 grams and measuring 4 cm. in its thickest area. The endometrial cavity was rough and shaggy and the myometrium contained many dilated vessels. Microscopic examination revealed hypertrophied myometrium with areas of decidual cells and dilated sinusoids. There was no evidence of malignancy nor tuberculosis.

Pathologic Diagnosis.—Postpartum uterus. Placenta accreta, partial.

Comment.—The premature separation of a lowly implanted placenta in this case can certainly not be charged to the presence of multiple sclerosis. The partial placenta accreta that was noted upon microscopic examination of the uterus also was not a direct result of this disease entity. Therefore, it must be concluded that the multiple sclerosis had no effect upon the course of the pregnancy. Conversely, it was not felt that the pregnancy in any manner affected the course of the disease. Multiple sclerosis is characterized by repeated exacerbations and remissions terminating eventually in death and in this particular case the symptoms that were noted during the prenatal course and the puerperium could very well have occurred despite the presence of the pregnancy.

This case has been presented because of Peckham's plea for the reporting of all cases of multiple sclerosis complicating pregnancy as well as for the rather unusual obstetrical course in the last trimester involving a premature separation of a low-lying placenta ultimately requiring a Porro hysterectomy with the delivery of a living child.

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SUCCESSFUL TERMINATION OF PREGNANCY WITH 116 DAYS OF RUPTURED MEMBRANES

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THIS case is presented because of the difficulties encountered prior to the premature rupture of the membranes, and of the passage of 116 days with continuous loss of amniotic fluid, terminated with the delivery of a normal (except for very mild bilateral talipes calcaneovalgus) living child. Premature rupture of the membranes need not terminate invariably with impending labor; it is possible to obtain fetal salvage.

Mrs. M. S., 31 years of age, was first seen in January, 1950, with a complaint of infertility. Her past history revealed an appendectomy 20 years previously and removal of a herniated intervertebral disc in 1947. Her menstrual history was normal. After ten years of marriage there had never been any pregnancy.

Physical examination including urinalysis and blood count was essentially normal except for the healed scars of the operative procedures, and a retroverted uterus. It was noted that the patient displayed a great deal of tension about her problem.

Her husband yielded an excellent semen specimen. After determination of a normal erythrocyte sedimentation rate, tubal insufflation demonstrated a curve of no patency. This was repeated one month later after sedative and antispasmodic therapy. This time the curve revealed a pressure of 200 mm. Hg maintained for the first two minutes of the application and then a sudden drop to 80 mm. Hg at which point a normal curve developed. This was followed very shortly by shoulder pain. In the meantime, the daily temperature chart was suggestive of normal ovulatory cycles, and advice was given accordingly as to a change in the couple's marital habits. The patient discontinued the remainder of the infertility investigation at this point.

She was seen again on Nov. 6, 1950, with a history of her last menses having occurred on Sept. 30, 1950, and with slight nausea, urinary frequency, and breast engorgement. Pelvic examination was deferred but the frog test was positive for pregnancy. Laboratory examination revealed Type B blood, negative Wassermann test, and an Rh-negative blood determination. The patient was elated and was now at ease.

On Dec. 15, 1950, the patient began to stain and was put to bed immediately and from then through the thirty-sixth week, she was treated with increasingly large doses of stilbestrol and buccal progesterone. The staining was never marked, was only occasionally accompanied by cramps, and occurred for the last time Jan. 1, 1951. Two weeks later, the uterus could be palpated abdominally, inspection of the cervix revealed no patency of the os and no bleeding, and the frog test remained positive. At this time the patient was allowed out of bed and placed on restricted activity. Quickening occurred at the end of January, 1951.

On Feb. 19, 1951 (21 weeks), the patient experienced a sudden flow of fluid per vaginam. She went to bed immediately but soaked the bed and several sanitary napkins that she wore. She continued to feel fetal movements but no fetal heartbeat could be distinguished. The fluid had an amniotic odor, was alkaline in character, and there was microscopic evidence of lanugo. No vaginal examination was done. Except for the initial flow, which was slightly blood tinged, there was never a steady flow but four to ten napkins were soaked daily, usually the lower figure. The uterus, which had been noted in a routine office visit four days previously to be at the umbilicus was now approximately three fingerbreadths below.

Expectant therapy of complete bed rest, of continuation of the hormonal therapy which had been instituted previously for the first-trimester bleeding, and of 600,000 units of oral penicillin daily was decided upon. She was kept well hydrated to provide for her normal needs and to replace approximately the abnormal fluid loss.

By March 5, 1951, the fetal heart was once more audible and the uterus was increasing in size and continued to do so from then on, though it never attained quite the size expected for the period of pregnancy. In April, 1951, there were two intervals of three and seven days, respectively, in which there was no apparent flow of amniotic fluid as determined by the dry sanitary napkins but on April 26, 1951, the leakage began again and continued till delivery. At 36 weeks the rigid bed rest regime was partially relaxed and the hormonal therapy was discontinued but the use of the oral penicillin was maintained. Abdominally, the fetus was in the left occipitoanterior position and apparently the vertex was engaged. This was confirmed by rectal examination which also revealed the cervix to be effaced. Braxton-Hicks contractions became frequent. The Rh determinations were repeated and were negative in the patient and positive in her husband, but repeated tests never revealed the presence of any agglutinating antibodies.

The patient was admitted to the Jamaica Hospital just before midnight of June 10, 1951 (the estimated date of confinement was July 7, 1951), because she thought she was in labor, but she did not develop active labor until 6 P.M. of the following day. The first stage lasted 7 hours, 10 minutes and the patient was delivered of a 5 pound, 11 ounce male infant with the aid of outlet forceps and a right mediolateral episiotomy, under light gas-oxygen-ether anesthesia, after an uneventful second stage of 50 minutes. Membranes covered the infant's head. Pitocin was administered at the delivery of the shoulders. In addition to a very short umbilical cord there was only a mild bilateral talipes calcaneovalgus present as an abnormality. Though the infant cried spontaneously, he had difficulty in breathing because of a great amount of mucus in the respiratory tract. This was relieved by aspiration but the baby was not well oxygenated until after he had been intubated.

The patient bled briskly in the third stage and it was necessary to remove the placenta manually. The placenta had already separated except for an attachment in the right cornu, which felt larger than the left (this was confirmed by hysterogram four months post partum). There was asymmetry of the uterine cavity in that the right cornu was longer and farther away from the sagittal plane of the uterus than the left cornu. Reconstruction of the membranes revealed that they had ruptured alongside the inferior pole of the placenta. Pathological examination of the placenta demonstrated no abnormalities.

The infant was treated as a premature. He was Rh positive and the Coombs test was negative.

The postpartum course was uneventful and mother and child left the hospital on the sixth day. The mother developed a cystitis several days later which responded well to chemotherapy and Pyridium. Her examination at six weeks was essentially normal. The child has progressed well in mental and physical development.

Comment.—It occurred to the author that this pregnancy carried on to a successful termination because of several reasons. The patient cooperated fully because of an understandable burning desire to have a live child after ten years of infertility; due to previous constant hormonal therapy administered because of the first trimester bleeding, the uterus was not responsive to the irritation caused by the loss of fluid; the rent in the membranes must have been very small, because, except for the first incident, there never was another gush of fluid but only a small constant dribble; and the use of antibiotics apparently was instrumental in preventing intrauterine inflammation and its catastrophic sequelae.

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AN UNUSUAL COMPLICATION FOLLOWING A BALDY-WEBSTER UTERINE SUSPENSION

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TWENTY-FIVE years ago the daily operating room postings of any gynecological service would almost certainly have included one or more uterine suspensions. However, within three decades gynecologists learned that many of these operations were unnecessary and others were incomplete, not relieving all of the patient's symptoms. Uterine suspensions now are carried out on only carefully studied and selected patients, and, performed under such circumstances, often afford great relief. In brief, a simple uterine suspension in most hospitals has become an unusual rather than an everyday procedure.

Formerly, many varieties of surgical technique were employed to correct the retro-displaced uterus. This writer believes that at the present time most gynecologists limit themselves to two uterine suspensions: the modified Gilliam and the Baldy-Webster, and that the modified Gilliam suspension is employed more often than the Baldy-Webster. At the Johns Hopkins Hospital suspensions other than the modified Gilliam are rarely seen.

However, the Baldy-Webster is still considered the suspension of choice by many eminent specialists among whom is Dr. Arthur Curtis. To be sure, this gynecologist recommends along with the Baldy-Webster operation the suturing of the uterosacral ligaments and posterior leaves of the broad ligaments and advancement of the bladder peritoneum upon the fundus. He does, however, treat the round ligaments almost exactly as Baldy and Webster advised fifty years ago.

This uterine suspension goes by the combined name Baldy-Webster because the publications of these two surgical pioneers appeared within such a short time of each other. The technique described in the two publications was strikingly similar even in small details. There was, however, one operative step described by Webster that Baldy did not mention although he also may have employed it—namely, to quote from Webster, "Each ligament [round ligament] is also stitched to the hole in the broad ligament." This sentence is of importance and should be emphasized. For when the operator does not make snug the openings in the broad ligaments around the round ligaments they may become larger in the years after the operation and may be the cause of some of the complications that have followed Baldy-Webster suspensions.

Before recording this case which shows a very unusual complication after a Baldy-Webster operation, I would like to refer to an article by Pemberton and Sager in which some of the more usual postoperative complications following the Baldy-Webster operation are discussed. The histories of two cases of intestinal obstruction due to loops of small intestine entering the holes in the broad ligaments and being caught there are presented in detail. A picture is shown of another case in which the uterus enlarged through the development of fibroid tumors in a woman who had several years previously had a Baldy-Webster operation. At the hysterectomy operation the holes which had been made in the broad ligaments were so large that the operator could easily introduce two fingers on either side between the round ligaments and the sides of the uterus.

The history and the findings in the case which the author wishes to report are the following: A 29-year-old white woman, complaining of pain in the right side of the lower abdomen, was admitted to his service at the Hospital for the Women of Maryland on Jan. 2, 1951. Her appendix had been removed when she was a child. Four years before he saw her a Baldy-Webster suspension for retroposition of the uterus had been carried out. She

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had been helped by this operation and for one year afterward had no complaints. She then became pregnant and following the birth of the child started having recurring pains in the lower abdomen, chiefly on the right side. There were no urinary or gastrointestinal symptoms and the menstrual history was normal. On the morning of January 2 she had an attack which was more severe than any she had had previously and her physician had her admitted to the hospital.

On admission the patient complained bitterly of lower abdominal pain and there was moderate tenderness on palpation over the lower right quadrant. On vaginal examination the patient was found to be bleeding moderately. This was not the correct time for her menstrual period. It was the first instance of irregular bleeding since she started having lower abdominal pains. The cervix pointed forward and was not softened. The uterus was in retroposition and was not enlarged. There was marked tenderness in the right fornix, but no definite abnormal pelvic mass was palpated. The temperature was 99.6° F., pulse was 110, respiratory rate 20, and the leukocyte count 12,000.
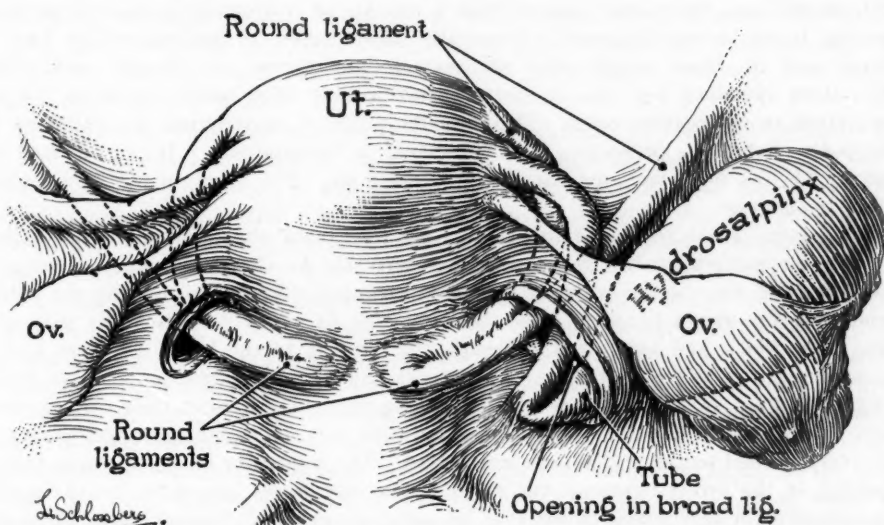

Fig. 1.—The pelvic organs viewed from behind. At operation the uterus was in deep retroposition, but in order to show the relationship of the tube to the round ligament on the right side the uterus was drawn as though it were in good position. On the left there is the opening in the broad ligament which was made during the Baldy-Webster suspension operation. At this second operation several years later the operator could introduce one finger easily through this opening. On the right it can be seen that the Fallopian tube, as well as the round ligament, has been drawn through the broad ligament. The distal part of the tube has been converted into a large hydrosalpinx. The point of constriction of the tube is shown.

The examiner did not feel that he could make a definite diagnosis. The possibility of an ectopic pregnancy was suggested by the vaginal bleeding, but there was no history of missed menstrual periods and the cervix was not softened. Salpingitis was, of course, considered, but there was no injection of the urethra or thickening of Skene's or Bartholin's glands, nor was there any history of leukorrhea. Smears and cultures for gonococci were negative. A normal intravenous pyelogram and a negative catheterized specimen of urine pretty well ruled out urinary pathology.

The patient was treated conservatively for forty-eight hours with rest in bed, penicillin and streptomycin. However, the pain in the lower abdomen did not lessen and the white blood count continued elevated. A laparotomy was decided on. A preoperative diagnosis is insisted on at the Women's Hospital so endometriosis was put down on the operative sheet. It seemed reasonable to suppose that contractions resulting from endometriosis had drawn the suspended uterus back into retroposition and that the abdominal pain was due to endometrial spilling from small ruptured cysts.

Operation, Jan. 4, 1951.—A lower midline incision was made. There were a few adhesions between the omentum and anterior abdominal wall as a result of the previous operation. These were easily freed. The appendix had been removed previously. The pelvic organs showed a remarkable picture. Although at the previous operation a Baldy-Webster suspension had been carried out, the uterus was now in complete retroversion. On the left side one could see where the broad ligament had been perforated and the round ligament passed through it and sewed to the posterior surface of the uterus. When this perforation of the broad ligament was made, either an unusually large opening had been made or the opening had gradually become larger following operation and pregnancy for it was now very easy for the operator to pass his finger through the opening. On the right side a more serious complication had developed and this was doubtless the cause of the patient's symptoms. After the opening in the broad ligament had been made, in the process of sewing the round ligament to the posterior surface of the uterus, the right Fallopian tube had apparently been dragged through this opening along with the round ligament. This brought about a condition in which the Fallopian tube, which normally lies posterior to the round ligament, passed over the round ligament with a knuckle of it protruding posteriorly through the opening in the broad ligament. Eventually, this knuckle of Fallopian tube had been constricted and its blood supply shut off until it was almost cut through and divided. Medially, there remained 4½ cm. of fairly normal-looking tube which ran from the point of constriction to the uterine cornu. Distal to the point of constriction the Fallopian tube was markedly distended, presenting the picture of a hydrosalpinx. It was dilated to a diameter of 2½ cm. and elongated until it measured 8 cm. The ovary on this side contained numerous simple cysts.

The operator freed the round ligaments from the points where they had been attached to the posterior surface of the uterus. On the left side he closed the large opening that had resulted from the uterine suspension with interrupted silk sutures, uniting the sides of the opening to the round ligament. On the right side by sharp dissection the part of the Fallopian tube which had been drawn through the opening in the broad ligament and was densely adherent to the broad ligament was freed and by gentle traction both it and the round ligament were drawn back through the opening until they were in their correct relative positions. A retrograde Rubin's test showed that the left Fallopian tube was patent and the left ovary normal so the left adnexa were saved. The right tube and ovary were removed. The opening in the broad ligament was closed. The uterus was suspended by the modified Gilliam method with care taken to see that no openings were left laterally into which loops of gut could enter. Care was also taken to see that the left tube was not pinched or twisted. The abdomen was closed in layers. The patient left the operating room in good condition and had an uncomplicated convalescence. It has now been eight months since she was operated on and she is having no trouble.

Comment.—The case just reported and the two recorded in 1929 by Pemberton and Sager show the necessity of a very exact technique in performing a Baldy-Webster uterine suspension. The walls of the openings made in the broad ligaments to permit the drawing through of the round ligaments must be sutured to the round ligaments. If this step in the operation is omitted, these openings may become larger as time goes by and loops of intestine become caught in these pockets causing intestinal obstruction to develop. It is also most important that the normal position of the tube not be disturbed in carrying out the suspension. When it is, such a complication as there was in this case may develop.

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MEDICAL ARTS BUILDING

MANAGEMENT OF ADDISON'S DISEASE DURING PREGNANCY WITH CORTISONE AND DESOXYCORTICOSTERONE

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F E. S., 30-year-old white para i, gravida ii, was referred to us on March 21, 1951, in her fifth month of pregnancy with a diagnosis of Addison's disease. She first reported to a doctor on Dec. 19, 1950, with the chief complaints of weakness, vomiting, and prostration. She gave the following history:

She had noted increased pigmentation on pressure areas of the body the latter part of 1949, and an increased tendency to sunburn. The pigmentation persisted through the winter and became more pronounced in the fall of 1950. In the past year and a half she had noted weakness, anorexia, and a 20-pound weight loss. Recently she had developed nausea and vomiting, intermittent generalized abdominal pain, and marked weakness. Her last menstrual period was Oct. 11, 1950.

Physical examination on admission showed blood pressure 90/50, weight 111 pounds. The patient was a tall, thin, dehydrated, youngish woman who appeared chronically ill. She had a diffuse dusky pigmentation, more marked on pressure areas; there were black freckles over the face and arms; the gums and buccal mucosa were deeply pigmented. The uterus was enlarged to the size of a two-month pregnancy. The rest of the physical examination at that time was essentially negative.

Laboratory examination showed serum sodium 124 meq. per liter, serum potassium 5.1 meq. per liter, nonprotein nitrogen 46.1 mg. per 100 c.c., fasting blood sugar 60 mg. per 100 c.c., serum chlorides 342 mg. per 100 c.c. The hemoglobin was 10.5 Gm.; red blood cells 3,840,000; white blood cells, urine, chest x-ray, kidney, ureter, and bladder were normal. The serologic examination was negative. Urine cultures, gastric washings, and guinea pig inoculations were negative.

Large doses (10 mg. a day) of desoxycorticosterone acetate were necessary before the patient began to improve. She was put on cortisone, and, when she came to us, was on 5 mg. DOCA by hypodermic daily, with 12.5 mg. of cortisone by mouth twice a day. Physical examination at that time showed most of the same changes present as in the original examination, except that the patient was in much better physical condition. The weight was 129 pounds and the patient had an apparently normal five-month pregnancy. Blood chemistry at this time was more nearly normal than on admission.

The patient was hospitalized until April 4, 1951, when she returned to her home in another state. She was readmitted on June 26, 1951, approximately 3 weeks before her estimated date of confinement, July 18, 1951. During this time she was on DOCA 5 mg. by hypodermic daily and 12.5 mg. of cortisone twice a day. On readmission her weight was 150 pounds, blood pressure 110/70. No edema or other abnormal symptoms or signs (except pigmentation) were present. All laboratory determinations were within a normal range. The fetus was nearing term size, engaged, in left occipitoanterior position. In the next four weeks the patient's blood pressure remained normal, ranging from 110/60 to 120/84. The dosage of cortisone was unchanged. The dosage of DOCA was gradually decreased to 1 mg. daily. On July 22, 1951, the presentation of the baby was found to be breech, double footling, right sacroanterior. Estimated fetal weight was 8 to 8½ pounds. The pelvis was gynecoid,

clinically and radiologically. She had had absolutely no sign of impending labor. A vaginal examination showed the cervix to be 1 cm. dilated, soft, and partially effaced. The membranes were stripped and labor induced with intravenous Pitocin in 5 per cent glucose. Two hundred c.c. of fluid containing 2 minims of Pitocin were given over a period of 5 hours. Until the membranes ruptured at 8 cm. dilatation, and the cord prolapsed, any marked slowing of the Pitocin resulted in cessation of contractions. One-tenth Gm. of Seconal and 50 mg. of Demerol markedly depressed the patient, slowing the pulse rate to between 50 and 56 per minute, and the respiratory rate to between 10 and 12 per minute. A breech extraction was done under ether analgesia, and a later pudendal block, with delivery of a normal, active 8-pound male infant.

The dosage of DOCA before, during, and after labor was unchanged, and remains 1 mg. per day (subcutaneously). The dosage of cortisone was as follows:

Day of delivery: At onset of active labor, 100 mg. intramuscularly, repeated in 12 hours.
First postpartum day: 50 mg. intramuscularly every 12 hours.
Second, third, and fourth postpartum days: 25 mg. (per os) every 6 hours.
Fifth and sixth postpartum days: 12.5 mg. (per os) every 6 hours.
Seventh postpartum day and thereafter: 12.5 mg. (per os) as 7 A.M. and 5 P.M.

The patient had an uneventful postpartum course, the blood pressure, pulse rate, respiratory rate, temperature, and laboratory determinations remaining normal. She was kept in the hospital for observation for three weeks. DOCA pellet implantation is planned for the near future.

CORTICAL VENOUS THROMBOSIS FOLLOWING DELIVERY

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PRIMARY thrombosis of the cortical veins is a very rare puerperal complication. It has been occasionally observed in association with extreme inanition, various toxic states, and general and local infections, but the literature contains only a few reports of the condition as a fatal puerperal complication. Cases have been reported by Symonds,[1] Mondre,[2] Davis,[3] and Martin and Sheehan.[4] All of the reported cases show definite clinical and pathological similarity.

Case Report

The patient was a 20-year-old parai, gravida ii. Prior to the first pregnancy which terminated in abortion at three months, she had received prolonged treatment for anovulatory sterility. Her last menstrual period was Dec. 12, 1949. During the first trimester of pregnancy, she received thyroid medication to prevent abortion. The pregnancy progressed normally until about the thirtieth week when there was a rise in blood pressure from 115/80 to 145/100, without albuminuria or edema. The membranes ruptured spontaneously, and a normally developed infant weighing 2,650 grams was delivered normally Aug. 24, 1950. The immediate postpartum course was afebrile and otherwise uncomplicated, and the patient was discharged from the hospital on the seventh postpartum day. The patient continued to be asymptomatic until Sept. 9, 1950, sixteen days post partum, when she complained of a peculiar sensation of numbness in the fingers of the left hand. After a night of fitful sleep, she awakened with a severe frontal headache and vomiting. Suddenly a left-sided convulsive seizure of short duration developed which was followed by recurring convulsive attacks. Her condition deteriorated to a left-sided status epilepticus associated with a temperature of 105° F. The respiration was rapid and stertorous. The convulsive seizures subsided with sedation. A lumbar puncture revealed an opening pressure of 280 mm. of water, 440 red blood cells, and 142 mg. per cent protein. Air studies showed no evidence of an intracranial mass lesion. Her general condition improved the following day to the point where she responded to simple questions but was otherwise lethargic. A left spastic-type hemiplegia was present. The right pupil was slightly larger than the left, but both reacted to light. Repeat lumbar tap was done, and the opening pressure was 250 mm. of water. Spinal fluid examination revealed 1,950 red blood cells, 10 white blood cells, and 96 mg. per cent sugar. A right carotid arteriogram done on the fourth day of the illness revealed no intracranial abnormalities.

On admission to the hospital, the blood pressure was 130/85, and remained within normal limits until near death. Urinalysis showed a specific gravity of 1.018, sugar positive, albumin 1 plus, and occult blood. Serologic tests for syphilis were negative. The blood count showed red blood cells 4,400,000, white blood cells 24,000, polymorphonuclear leucocytes 80 per cent, lymphocytes 20 per cent. On Sept. 16, 1950, total leucocytes were 5,000, blood calcium 10.5 mg. per cent, nonprotein nitrogen 39 mg. per cent, and blood sugar following intravenous glucose was 186 mg. per cent.

The patient remained oriented and responsive until the seventh day, when she gradually became comatose with a bilateral flexion spasticity of the upper extremities and extensor spasticity of the lower extremities. No change was noted following stellate blocks. Anticoagulants were not used because of the persistence of blood in the spinal fluid. The patient died without regaining consciousness on Sept. 21, 1950, twelve days after the onset of the illness.

An autopsy revealed the following findings: There was an extensive bilateral thrombosis of the large cortical veins. The superior sagittal sinus and both lateral sinuses contained thrombi which on the right extended into the jugular vein. In the right frontal lobe, there was a large area showing early necrotic changes. Numerous areas of hemorrhagic necrosis were associated with the thrombosed veins. A few small pulmonary emboli were found in the lower lobe of the left lung. The postmortem examination was otherwise noninformative.

Comment

In this case, the onset of headaches and unilateral seizures was undoubtedly associated with thrombi formation in the cortical veins overlying the right cerebral hemisphere. With extension of the clot to the sagittal and lateral sinuses, there was a subsequent rise in the intracranial pressure as is indicated by the spinal taps. Air studies ruled out the possibility of an intracranial mass lesion, such as a brain tumor or an intracerebral hematoma. The possibility of a vascular anomaly or aneurysm was unlikely in view of normal angiographic findings. Satisfactory venograms were not obtained. Subsequent progression to involvement of the opposite extremities and an ultimate decerebrate state were indicative of a widespread venous thrombosis involving both hemispheres and the sagittal sinus. The exact cause of thrombus formation in this condition is not known, although various mechanisms have been hypothesized. It has been suggested that slowing of the venous flow or some alteration in the clotting mechanism of the blood following pregnancy may be factors leading to thrombus formation. Another possible explanation is suggested by Martin[5, 6]: He cites the work of Batson,[7] who postulated that an embolus could be dislodged from a pre-existing thrombosis of the pelvic veins and be transmitted to the brain via the vertebral vein system.

The prognosis is favorable if the thrombosis is confined to the veins overlying one hemisphere, but if the pathological process spreads to the other hemisphere or to the sagittal sinus, the outcome is usually fatal. The differential diagnosis of this disorder occurring in the puerperium must cover all conditions that cause convulsive seizures and paralysis whether or not peculiar to pregnancy. The treatment consists of the control of the seizures by sedation, general supportive measures, and anticoagulant therapy.

Summary

A case of cortical venous thrombosis following pregnancy is reported. This is a very uncommon puerperal complication but does occur frequently enough to be considered when neurological symptoms appear during the puerperium. The outstanding features of the disease are described as sudden onset of headache, convulsive seizures, and paralysis several days following delivery. The relationship of the clinical course to the pathological process is briefly discussed.

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104 SOUTH MAIN STREET

HEMANGIOPERICYTOMA

An Unusual Pelvic Tumor

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M RS. C. S., aged 40 years, white, married three years, no pregnancies, was first seen Dec. 14, 1949, with chief complaint of lower abdominal pain and rectal and vaginal pressure.

She was well until July 2, 1949, when she experienced an attack of sharp cramplike abdominal pain associated with rectal tenesmus and a diagnosis of ovarian cyst with a twisted pedicle was made by her doctor and operation advised. However, symptoms were relieved and the patient refused surgery. On Nov. 20, 1949, the symptoms recurred and persisted intermittently until the date of admission to hospital.

Menstrual History.—Menstruation began at 13 years of age, every 28 days, lasting 5 days, with no dysmenorrhea. The last menstrual period was Dec. 6, 1949.

Past History.—There was congenital dislocation of the left hip. Dilatation and curettage and myomectomy had been done in 1936; appendectomy in 1938.
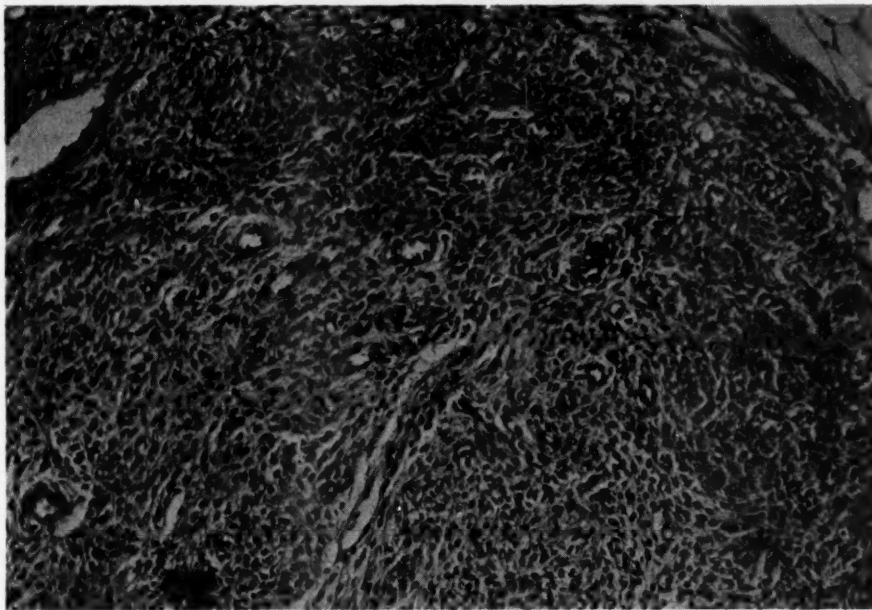

Fig. 1.—Section through omental nodule removed at operation. (Hematoxylin and eosin stain.)

Physical Examination.—She was a well-nourished woman with marked deformity of the spine and left hip. There was a lower midline scar in the abdomen. The vulva and vagina were normal. The cervix was smooth, the corpus slightly enlarged, anterior, and fixed in this position. A 6 cm., firm mass in the cul-de-sac was making pressure on the anterior rectal wall.

Laboratory Findings.—Serology negative; hemoglobin 12 Gm.; red blood count 4,240,000; white blood count 8,500; sedimentation rate, within normal limits; urinalysis normal.

X-ray Findings.—X-ray of the lower bowel on Dec. 16, 1949, showed no filling defect and no evidence of abnormality of the terminal ileum and colon.

Operative Procedure and Findings.—At operation, there were numerous adhesions and several small cystic accumulations of the terminal portion of the omentum which was adherent to a thick-walled cystic mass, about 5 cm. in diameter, in the cul-de-sac. This mass was densely adherent to the rectosigmoid and was dissected free with considerable difficulty. The bed of this mass was quite hemorrhagic and Gelfoam was packed into this area to control bleeding. The terminal portion of the omentum was resected. The uterus and adnexa seemed normal. The patient made a good immediate postoperative recovery.

Pathological Report.—The specimen was an opened cystic structure containing doughy, cheesy material and measuring 4 to 5 cm. in diameter. The contents were yellow in color.

Microscopic.—Sections through the omental nodules (three) showed that all had the same cytologic picture. The process appeared neoplastic and the tumor was composed of rather uniform cells with round, oval, and spindled nuclei and a sparsity of cytoplasm. These cells have a perivascular whorling and may be originating from vessels (pericytes of Zimmerman). The mass from the cul-de-sac is almost completely necrotic except for a small rim of tissue at the periphery which resembles that described above.

Diagnosis.—Hemangiopericytoma in the omentum and cul-de-sac.

Follow-Up.—Examinations disclosed persistent induration in the cul-de-sac and on Nov. 5, 1950, a 5 cm. indurated mass was felt protruding into the anterior rectal wall. Sigmoidoscopy revealed a lesion protruding into the rectum about 10 cm. above the anorectal line. This lesion, which seemed to be a conglomeration of tiny cysts, was biopsied.

The pathologist reported, ''The small portion of tissue shows loss of mucosa on one surface with protrusion of granulation tissue on the surface. Beneath the mucosa, there is compact tissue composed of light staining, equal size, small, oval-shaped nuclei showing a few fibrillar processes. Many blood vessels are noted. *Diagnosis:* Hemangiopericytoma of rectum. *Comment:* The previous biopsies in this case were reviewed and the histologic picture appears quite similar to that seen in this biopsy.''

The patient remained asymptomatic throughout the follow-up period. However, in view of this definite evidence of recurrence, she was referred to a general surgeon for resection of the lower bowel.

Summary.—We have reported a rare pelvic tumor. Although, at the original operation, the mass was a benign-looking, well-encapsulated, cystic tumor, there evidently were enough tumor cells remaining to allow for recurrence and invasion. This is another evidence of the malignant tendencies of hemangiopericytoma.

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Department of Reviews and Abstracts

Selected Abstracts

Anatomy, Anomalies

Carlsen, C. J.: **A Case of Supernumerary Ureter Opening Extravesically,** Acta obst. et gynec. Scandinav. **30**: 439, 1951.

A single case report of a 17-year-old girl who suffered from periodic urinary incontinence beginning in infancy is presented. On gynecological examination, no abnormalities were found. Cystoscopy showed regular periodic oozing of drops of clear fluid from a small opening immediately below the lower part of the urethral orifice on pyelography, this proved to represent the opening of a supernumerary left ureter. Laparotomy was performed, and the supernumerary ureter was isolated deep in the pelvis, divided after ligation of the peripheral end, and implanted into the bladder by the Sampson-Krönig method. Postoperative recovery was uneventful.

Supernumerary ureter opening extravesically has a reported incidence of approximately 1 in 80,000 cases of urological disorder. About 90 per cent of cases diagnosed in vivo have occurred in the female, since the anomaly rarely gives rise to clinical symptoms in the male. The etiology is thought to be some disturbance in the ureteric anlage before it grows toward the renal anlage; two ureteric buds appear on the dorsal aspect of the Wolffian duct in the third or fourth week of embryonic life instead of one. Failure of the anomalous ureter to open into the bladder results from failure of detachment of the primitive ureter from the Wolffian duct before the sixth embryonic week. Infection in the abnormal segments of the urinary tract is the rule in such cases, and accounts for one group of the characteristic symptoms, the other group being related to disturbances of micturition. The patient reported here complained that a gush of urine would escape when she would get up after sitting or lying down for a reasonably long time; the explanation of this phenomenon is that the urine presumably collects in a saclike dilatation which is almost always present above the opening. In some of the reported cases, incontinence was absent; this finding was reported only in those patients in whom the aberrant ureter opened proximal to the sphincter. Methods of therapy, all surgical, include vaginal and abdominal implantation of the ectopic ureter into the bladder, anastomosis between the principal and supernumerary renal pelves, ligation of the supernumerary ureter, heminephrectomy, and total nephrectomy. The author emphasizes the basic principle of maintenance of a maximum of functional renal parenchyma, and remarks upon the almost uniformly favorable prognosis in properly treated cases.

DOUGLAS M. HAYNES

Anesthesia, Analgesia

Torkelson, Harold P., and Cooley, Chester L.: **Single Dose Low Spinal Anesthesia in Obstetrics,** West. J. Surg. **59**: 533, 1951.

Regional anesthesia in the form of saddle block or low spinal anesthesia continues to enjoy a vogue in some well-established obstetrical departments. This report deals with 4,000 women who were delivered under single dose spinal anesthesia. A new drug,

Cyclaine, in a 10 per cent hyperbaric glucose solution which has been used to weight the anesthetic agent, is discussed. The dose is approximately 1 c.c. or 25 mg. of Cyclaine administered when the cervix is completely or nearly completely dilated and the present-ing part at the ischial spines. A long 22-gauge spinal needle is introduced into the sub-arachnoid space through the third or fourth lumbar interspace. The injection is made with the patient in the sitting position and the contents of the syringe emptied quickly into the spinal canal. About 30 seconds are allowed for the solution to gravitate and then the patient is put in a low Fowler's position for 10 minutes after which time the anes-thetic agent is fixed and the patient may be placed in any convenient position for delivery.

Immediately after the spinal anesthetic was given intravenous fluids were started and continued throughout the operation. Morphine was routinely given following the delivery of the baby. All patients received penicillin for at least the first four post-partum days.

The most common complications were postspinal headaches and urinary retention. It is felt that the incidence of postspinal headache can be reduced by the routine ad-ministration of fruit juice to patients in labor to insure adequate fluid intake, the use of a small-gauge spinal needle, spinal puncture performed with the bevel of the needle in a vertical position to avoid cutting the dura, use of only perfect needles, the washing of all needles and syringes thoroughly and sterilization by autoclave instead of boiling, and the use of a separate needle to withdraw the anesthetic agent from the ampule.

The authors believe that Cyclaine is a superior anesthetic agent to Metycaine. When it is employed only a small number of patients require ephedrine to combat a falling blood pressure. A comparatively low dose of the drug is required and the best results are obtained when the drug is administered in a 10 per cent solution of glucose.

From the reading of this article one would get the impression that spinal anesthesia for delivery is a most innocuous procedure. Unfortunately, this is not the universal experience.

                                                                                WILLIAM BICKERS

Javert, Carl T., and Hardy, James D.: Influence of Analgesics on Pain Intensity During Labor (With a Note on "Natural Childbirth"), Anesthesiology 12: 189, 1951.

In this article the authors have considered the effects of various analgesic agents on the "pain intensity of normal patients during labor." Pain in labor was studied for the first time by using the Hardy-Wolf-Goodell dolorimeter, which is an instruument for measuring "pain threshold" and "pain intensity" as expressed in "dols." Twenty-six patients were studied before analgesia, 21 primiparas and 5 multiparas. After several hundred preliminary measurements, 19 patients were given 26 injections of various anal-gesics, such as morphine, scopolamine, Demerol, heroin, and apomorphine, including various combinations of these drugs. The effects of these analgesic agents were compared but varied somewhat in degree. "Pain threshold" was raised and "pain intensity" lowered; duration of contractions, interval between contractions, degree of restlessness, and com-plaints of pain "here, there, and yonder," and degrees of amnesia were all related to the total amount of agent given and to the interval at which it was administered. The skin "pain threshold" was not raised nor lowered during the antepartum period, during labor, or in the puerperium. The "pain threshold" of the cervix was not investigated for obvious reasons. The dolorimeter can be used to measure quantitatively "pain threshold" and "pain intensity" in labor but it is too complicated and time consuming for routine use in obstetrics.

                                                                             HARVEY B. MATTHEWS

Fuchs, F.: Spinal Anesthesia as a Treatment of Postpartum Atony of the Uterus, Acta obst. et gynec. Scandinav. 30: 384, 1951.

Spinal anesthesia with Novocain was used as a method of treatment of postpartum hemorrhage due to uterine atony in 10 patients whose total blood loss varied from 800

c.c. to 1,900 c.c. The rationale of the method is derived from the experimental observations of Whitehouse and Featherstone, who found that the effect of spinal anesthesia on the rabbit uterus is one of stimulation of contraction of the circular muscle bundles and of relaxation of the longitudinal muscle bundles, presumedly because of paralysis of the parasympathetic fibers. The contraction of the uterus following performance of spinal anesthesia was found to last some two hours, and seemed to be of vital assistance in the control of hemorrhage which had been proved refractory to the usual oxytocic drugs. It is recommended that the method be used before the blood loss exceeds 750 c.c., or if the blood pressure begins to fall. The hypotensive effect of the spinal anesthetic itself is readily controllable by vasopressor drugs. The author emphasizes that the method is no substitute for replacement of blood loss by transfusion, but states that pre-existing shock does not absolutely contraindicate use of the method. If, in spite of the use of this treatment, hysterectomy becomes necessary for hemostasis, it can be performed promptly without further anesthesia.

DOUGLAS M. HAYNES

Cesarean Section

Jacobson, Philip: Improved Uterine Closure in Classical Cesarean Section, West. J. Surg. 59: 431, 1951.

The low cervical cesarean section has largely superseded the classical operation. However, the classical operation yet has a place in the treatment of those cases in which speed is essential for the preservation of life in mother or child. The high incidence of complications following the classical operation and their comparative absence after the low flap operation have resulted from a faulty method of closing the uterine wound rather than the anatmical site of the incision in the uterus. The complications are said to be caused by the large quantity of catgut inserted in a wound that will shrink to less than one-third its original size before the absorption of the suture material is completed. The mass of catgut is forced into a relatively small tissue area and becomes a foreign body threatening the integrity of the uterine wall by strangulating and displacing the muscle fibers.

An improved techniquue for the closure of the classical incision is described. It consists of a few stay sutures and a continuous inverting suture along the peritoneal surface. Four to six stay sutures are placed through and through the uterine muscle and left untied. An inverting suture of chromic catgut closes and invaginates the peritoneal surface of the uterus. When the uterus is completely contracted the stay sutures are tied over the inverting peritoneal layer. This technique leaves no buried knots within the myometrium and the tissues are approximated with a minimal amount of strangulation.

The author reports on sixty-one consecutive cases so treated without morbidity. In four patients who had repeated cesarean sections the scars were barely noticeable.

WILLIAM BICKERS

Schluter, Hans F.: Cesarean Sections at Sutter Maternity Hospital, West J. Surg. 59: 330, 1951.

From the Sutter Maternity Hospital comes the report covering 29,843 deliveries between 1938 and 1950. Delivery was accomplished spontaneously in 73 per cent, by forceps in 22 per cent, there were 0.5 per cent delivered by breech extraction, and the incidence of cesarean section was 2.6 per cent. There were two maternal deaths in the 820 patients delivered by cesarean section. One of the deaths occurred following the classical operation and one following the low cervical operation. There were 44 fetal deaths giving a mortality in the cesarean section group of 5.34 per cent. The corrected fetal mortality, after deducting the prematures and stillborns, was 4.3 per cent.

Indications for the operation were in the order of frequency: previous cesarean sections, dystocia, hemorrhage, heart disease, toxemia, diabetes, erythroblastosis fetalis, history of difficult labor, and elderly primipara.

In his conclusions the author makes a plea for the more liberal use of cesarean section but the statistics quoted from his hospital indicate a most conservative attitude.

WILLIAM BICKERS

Malignancies

Laborde, Simone: The Treatment of Choice for Stage One Carcinoma of the Cervix, Gynéc. pratique 2: 141, 1951.

Laborde, at the International Cancer Congress in Paris, 1950, reports on a series of 28 patients with Stage I cervical carcinoma who had received postradiological hysterectomies done at the Curie Foundation of the Gustave Roussy Institute in Villejuif (just outside Paris) in the preceding two years. He notes first that their general results calculated as "average of cures," after a period of 5 to 20 years, amounts to 70 per cent, a far higher figure than the one obtained by the Wertheim operation which was formerly used.

Laborde further observes that "the great interventions which are now practiced nowadays in the United States yield a percentage of survivals which is well under and below the rate obtained by radiological methods since the statistics of Bonney do not show more than 40 per cent of 'cures' after 5 years and Meigs, the most convinced partisan of the radical operation which he considers the only rational treatment to eradicate glandular metastasis, does not obtain more than 36 survivals of 99 cases after a period of 3 years, or 36.33 per cent."

Laborde observed that of the 28 women hysterectomized following radiological therapy there were 25 specimens of uteri in which no residual carcinoma could be demonstrated pathologically.

The author concludes that in his opinion radiological treatment of carcinoma of the cervix yields better results and he is of the impression that in adding hysterectomy and lymph gland dissection operations in previously radiologically treated cases we are not on the right road to progress.

CLAIR E. FOLSOME

Miscellaneous

Bergman, Per, and Werner, Ivar: Analysis of Carbohydrates in Human Cervical Mucus by Means of Paper Partition Chromatography, Acta obst. et gynec. Scandinav. 30: 273, 1951.

Human cervical mucus was analyzed at various phases of the menstrual cycle for determination of its carbohydrate content by means of a paper partition chromatography technique. The carbohydrate composition of cervical mucus did not show appreciable cyclic variations. Regularly identified carbohydrates were galactose, glucose, mannose, fucose, and a hexosamine which proved to be predominantly glucosamine. The composition of the polysaccharide most frequently encountered was similar to that of blood group specific substances, and to that of neutral polysaccharides derived from various other sources of epithelial mucus. The observed glucose fraction is probably derived from a glycogenic admixture of possibly endometrial origin. Such a local glycogenolysis might provide an energy source for spermatozoa in contact with cervical mucus, although previous studies have shown that mannose and fructose may also serve as substrates for spermatozoal metabolism.

DOUGLAS M. HAYNES

Bergman, Per, and Lund, Carl G.: The Osmotic Pressure of Human Cervical Mucus, Acta obst. et gynec. Scandinav. 30: 266, 1951.

The osmotic pressure of human cervical mucus was determined at various times during the menstrual cycle, using a method involving galvanoscopic comparison of evapora-

tion rates of mucus as compared with those of standard saline solutions. The osmotic pressure of cervical mucus during the ovulation phase was found to correspond with that of normal saline, while at other times during the cycle the pressure of the mucus was greater. The effect of changes in osmotic pressure on spermatozoal motility was then studied by adding diluted semen to constant amounts of sodium chloride solutions of various known concentrations, and comparing spermatozoal motility of these preparations. The percentage of motile spermatozoa was found to be greatest in solutions of 0.9 and 1.2 per cent sodium chloride. These concentrations correspond to the osmotic pressure range of cervical mucus during the ovulation phase as previously determined. When, therefore, spermatozoa leave spermal plasma and enter cervical mucus during the ovulatory phase, they are not exposed to changes in the environmental osmotic pressure which are present at other times during the cycle. This factor may contribute to maximum fertility at this time.

DOUGLAS M. HAYNES

Wexler, Irving B., and Wiener, Alexander S.: Blood Group Factors and Physiological Icterus, Brit. M. J. 1: 1228, 1951.

The authors feel that the course of physiological icterus resembles so closely the course of erythroblastosis caused by mild sensitization to the Rh factor that the possibility has to be considered that they may have the same pathogenesis. They present studies on the icterus index, red cell count, and hemoglobin concentration, as well as the A-B-O groups, M-N type, and Rh-Hr types of 21 newborn infants selected at random.

Maternal and infant bloods were examined each day for the first five days of life. Cases were divided into two groups depending on whether the A-B-O group and the Rh types of the infant were compatible or incompatible with those of the mother. The average icterus index of the cord serum of the compatible group was 10.8 units and of the incompatible was 9.2 units. In both groups the icterus index usually rose soon after birth and at the highest point the average index was 36.8 units in the compatible group and 30.9 units in the incompatible group. Such results indicate that the high icteric index of the neonatal period are not ascribable to incompatibility of the A-B-O groups or the Rh types. Values for blood counts and hemoglobin remained constant, indicating that the rise in the index was not due to hemolysis.

Inadequacy of the excretory function of the liver has been shown to be one of the phenomena associated with physiologic icterus, but the cause for this malfunction has not been determined. Wiener has postulated a pathogenesis on an analogous basis. Women at term demonstrate the presence of autoantibodies in their serum. These are of the univalent variety, so are presumably capable of traversing the placental barrier and coating the fetal red blood cells. Since the antibodies are of the cold variety, the cooling of the baby's skin at birth brings about clumping of the coated red cells and acts as the trigger mechanism that sets off the explosion that is physiological icterus.

JOHN T. COLE

Newborn

Epstein, Harold C., Hochwald, Adolf, and Ashe, Rosemary: Salmonella Infections of the Newborn Infant, J. Pediat. 38: 723, 1951.

This report of two outbreaks of Salmonella infection in the newborn infant, one due to S. oranienburg and the other due to S. bareilly, is from the Departments of Pediatrics and Laboratories, Mount Sinai Hospital of Cleveland, and the Departments of Pediatrics and Pathology, Western Reserve School of Medicine.

The first outbreak, due to S. oranienburg, affected eighteen of the thirty-four exposed infants. There were three fatalities. The signs were, in order of frequency, diarrhea, emesis, shock, leucocytosis, cyanosis, acidosis, nitrogen retention, and anuria.

Aureomycin was ineffective against *S. oranienburg* in doses of 25 mg. per kilogram. It may have been somewhat effective against *S. bareilly.*

Epidemiological studies demonstrated that conclusions concerning the causation of a Salmonella outbreak can be drawn only after complete identification of the organisms is made in all cases. Many of the personnel were found to be harboring Salmonella strains unrelated to those causing infection in the infants.

In one outbreak, *S. oranienburg* was found in the water of a bottle warmer used to reheat the milk. An electrician called in to repair the instrument remembered having had a short attack of enteritis at the time of his work at the hospital.

The authors assert that periodic cultures should be done at regular intervals on stools of all personnel assigned to the nursery, pediatric service, and milk-formula kitchen.

<div align="right">JAMES P. MARR</div>

Laupus, William E., and Bousquet, Franklyn P., Jr.:   Retrolental Fibroplasia.   The Role of Hemorrhage in Its Pathogenesis. Am. J. Dis. Child. 81: 617, 1951.

This study of retrolental fibroplasia is from the Departments of Pediatrics and Surgery (Ophthalmology) of the New York Hospital-Cornell Medical Center in New York City.

Serial ophthalmoscopic examinations on 72 premature infants weighing less than 1,650 grams at birth have established the importance of hemorrhage as a precursor of the fully developed disease.

The theory of postnatal development of retrolental fibroplasia is supported by the absence of serious ophthalmologic abnormalities from all infants at the initial examination.

The features characterizing the normal premature fundus, especially the existence of a sharply defined pale peripheral zone of retina, are described.

In 13 of 14 infants in whom retrolental fibroplasia developed, a consistent pattern of pathogenesis from the first stage of minimal retinal vessel changes through each of five succeeding stages, preretinal hemorrhage formation, extension of these hemorrhages into the vitreous, organization of the hemorrhages with angiofibrous proliferation, subsequent retinal detachment, and the formation of a retrolental membrane, has been observed.

The high incidence of serious ophthalmologic abnormalities, despite supplementation with vitamin E, challenges the prophylactic role attributed to the tocopherols in treatment of this disease.

Conclusion: Postnatal intraocular hemorrhages are common in small premature infants, and retrolental fibroplasia is a sequel to these hemorrhages.

<div align="right">JAMES P. MARR</div>

Stiennon, O. Arthur: Pneumatosis Intestinalis in the Newborn, Am. J. Dis. Child. 81: 651, 1951.

The first account of this extremely rare condition is usually attributed to Bang, who reported an autopsy case in 1876. It seems, however, that earlier accounts of the condition were in existence, namely, Mayer's description in 1825, and the still earlier report (1730) of the anonymous Russian author I. G. D., cited by Combalousier.

Maass, in 1904, described the first reported case in a child. The diagnosis of pneumatosis was first established at autopsy. Moreau, as early as 1917, predicted that eventually a preoperative diagnosis would be made on the basis of the roentgenologic appearance of the abdomen. Reverdin was able to fulfill this prophesy in 1924, and his diagnosis was confirmed by laparotomy.

Since the roentgen appearance of pneumatosis intestinalis, or intestinal emphysema, in children has not previously been reported, the authors present two such case records with accompanying photomicrographs revealing the characteristic ring-within-ring shadows of the inflated bowel.

The protean manifestations of interstitial gas are collected, and a unified theory which gives a reasonable account of its genesis is introduced.

JAMES P. MARR

Placenta

Naeslund, John: **Studies on Placental Permeability With Radioactive Isotopes of Phosphorus and Iron**, Acta obst. et gynec. Scandinav. 30: 231, 1951.

In his studies of placental permeability, the author used radioactive phosphorus P^{32} and the radioactive isotope of iron Fe^{39}. The experiments with radioactive phosphorus involved the transfer of maternal blood to a paraffinized flask containing radioactive phosphorus, washing of the red cells tagged in this manner, and their reinjection ten minutes before anticipated delivery. Cord- and maternal-blood samples were collected after delivery, and specific radioactivity was measured in maternal and fetal red cells, plasma, and whole blood by means of a Geiger-Müller tube. The use of this technique results in the conveyance into the maternal blood stream of 25 to 35 per cent of radioactive phosphorus mixed with the treated blood sample.

Naeslund reports that, in his experiments with radioactive phosphorus, the specific radioactivity of the fetal red cells was consistently very low, many of the determinations falling within the limits of experimental error. The maternal blood usually showed a comparatively high degree of specific radioactivity; maternal plasma values were much lower. None of the results with phosphorus offered any concrete evidence that radioactivated blood cells from the mother had been transferred to the fetal vascular system, although, as the author emphasizes, these results do not preclude the possibility of earlier leakage through the placental barrier.

In the second series of experiments, radioactive iron in the form of ferric chloride was injected into polycythemic patients from whom, after 14 days, blood was withdrawn and transfused into pregnant women whose deliveries were anticipated within one week. During delivery, samples of maternal and cord blood were collected, and radioactivity of the contained iron determined by plating out the iron in a specially designed electrolysis apparatus. By this method, the maternal red cells usually registered rather high specific radioactivity, and the plasma a rather low value. All the figures for whole blood were higher than the sum of the specific radioactivities of corpuscles and plasma. The specific radioactivity of blood samples from the child was considerable in this experimental series, in contrast to the results obtained using radioactive phosphorus. In some of the experiments in which there was high specific radioactivity of the child's red cells and virtually none of the mother's, it is possible to theorize that some of the strongly radioactive fetal red cells may have crossed the placental barrier.

The author cautiously concludes that occasionally at the end of pregnancy or during labor there may be leakage of substances or blood corpuscles across the placental barrier from maternal to fetal blood streams and vice versa. Additional evidence in support of such a contention can be collected from the literature, where histologic studies of placentas and experiments using radioactive sodium and heavy water have occasionally suggested similar conclusions.

DOUGLAS M. HAYNES

Pregnancy, Physiology

Miller, George H., Jr., Davis, M. Edward, King, Albert G., and Huggins, Charles B.: **Serum Proteins in Pregnancy**, J. Lab. & Clin. Med. 37: 538, 1951.

This presentation briefly reviews the literature concerning serum protein change in normal pregnancy; it emphasizes the relatively slight decline in serum protein, but the significant drop in albumin, which is compensated by a rise in alpha and beta globulins.

These workers studied protein phenomena in normal pregnancy by a micro-Kjeldahl technique for serum proteins which yielded results similar to those of other groups. They studied the albumin defect by a thermal coagulation test and phenolsulfonephthalein binding properties which they claim to be relatively simple and precise. Again, they were able to confirm previous reports that the albumin decline starts in the third month and becomes more abnormal as pregnancy advances. In most cases the total protein of maternal serum was higher than that of fetal serum, while the reverse was true for albumin.

The authors suggest that the endocrine changes of pregnancy may be responsible for the protein alteration.

S. B. GUSBERG

Salfelder, Von K., and Lambertz, H. J.: Concerning the Question of Superfetation, Geburtsh. u. Frauenh. 11: 50, 1951.

The question as to whether a woman is able to ovulate and become pregnant while she is already gravid has never been answered satisfactorily. The authors describe a case of what they believe to be superfetation in a human being, and cite 27 other cases from the published literature believed to be similar. The case cited is that of a German woman, who, in Nevember, 1949, was delivered of two fetuses, one 14 cm. and the other 9 cm. in length. The only unusual fact in her history was that, although she knew that she was pregnant, she bled similarly to a normal menstrual period in August, 1949. The two embryos were in separate amniotic sacs, and were delivered separately. Both the gross and microscopic studies demonstrated a different period of development. The placenta, likewise, was much further developed and more differentiated in the larger child. From this case, as well as from those cases cited in the literature, the authors believe that the condition of superfecundation and superfetation does occur in human females at times.

L. B. WINKELSTEIN

Pregnancy, Toxemia

Rasmussen, Håkon, Bøe, Finn, and Müller, Ottar: Late Prognosis of Eclampsia, Acta obst. et Gynec. Scandinav. 30: 256, 1951.

A follow-up examination of 143 eclamptic patients, covering a period, in each case, of from 10 to 18 years following the eclamptic episode, was undertaken with the purpose of investigating posteclamptic sequelae, including those of posteclamptic hypertension. One woman, representing 0.8 per cent of the patients, died of cardiorenal disease a year and a half after the attack of eclampsia. In 70 women, or 59 per cent, the blood pressure and urine were normal. Moderate hypertension was observed in 23 patients (19.5 per cent), and more severe hypertension in 18 women, or 15 per cent, totaling 42 cases of persistent hypertension (35.6 per cent). There was no case of posteclamptic chronic nephritis. Proteinuria, when present, was of the inconstant type characteristic of essential hypertension. Severe hypertensive sequelae occurred chiefly in patients with high blood pressure levels, as might be anticipated. One woman had a cerebral hemorrhage, and four showed left ventricular enlargement with congestive heart failure. Moderate left ventricular hypertrophy without signs of failure was encountered in 5 patients. On investigation of the variability of the posteclamptic hypertension by means of functional tests (Amytal test, nitrite test, and hourly blood pressure curves), it was found that the blood pressure reached normal levels at one time or another in all but three of the patients studied. It appears that blood pressure lability is a characteristic feature of the hypertension which follows eclampsia, and the authors postulate that this lability may explain the relative infrequency of serious cardiac, renal, and cerebral disorders later in life.

DOUGLAS M. HAYNES

Mukherjee, C. L., and Govan, A. D. Telford: Blood-Pressure and Prognosis in Toxemia of Pregnancy, J. Obst. & Gynaec. Brit. Emp. 57: 941, 1950.

Recently attention has been focused upon hypertension that usually goes along with the toxemias of pregnancy in an effort to explain its etiology and its relationship to the toxemic symptoms. It is a well-known fact that symptoms may be equally severe at blood pressures varying from 140 to 190 systolic and that not infrequently a pressure of 190 gives only mild or no symptoms. Convulsions and/or accidental hemorrhage may occur at all levels of hypertension. The diastolic pressure is often a better guide to prognosis and its elevation is more commensurate with the severity of the toxemic symptoms. But here also inconsistencies exist. Nevertheless, hypertension, as manifested by the relationship of systolic and diastolic pressures, is the earliest manifestation of the toxemic state and measurement of this hypertension is the simplest method of recording the progress of the patient. Therefore it becomes necessary to find some means of analyzing these readings in order to help us in clinical management and prognosis.

In surveying their material of 936 cases, the authors divide them into 5 clinical groups as follows: Group I, hypertension without toxemia in late pregnancy; Group II, hypertension throughout pregnancy with toxemic manifestations during the last trimester; Group III, toxemia in the last trimester without preceding hypertension; Group IV, hypertension and eclampsia; and Group V, hypertension and retroplacental hemorrhage. Clinical manifestations are given for each group and tables are appended showing the systolic: diastolic ratio for these groups.

In their summary, the authors direct attention to the following: ''(1) the results indicate that the hypertension of toxemia is diastolic in origin; (2) the hypertension remains balanced during pregnancy in cases of essential hypertension unless the pregnancy is further complicated by toxemia; (3) the systolic:diastolic ratio in essential hypertension remains at 1.7 or more. In toxemia the hypertension is unbalanced and the ratio falls below 1.7. This provides an additional means of differentiating essential hypertension from toxemia and also indicates when toxemia has been superimposed on simple hypertension; (4) as the ratio falls toxemia manifestations become more severe and complications such as eclampsia tend to occur if the ratio drops below 1.5; (5) a rapid fall in ratio over a matter of hours occurs before the onset of retroplacental hemorrhage.''

HARVEY B. MATTHEWS

Puerperium

Deacon, A.: Spontaneous Intraperitoneal Rupture of the Bladder in the Puerperium, Brit. M. J. 1: 508, 1951.

Spontaneous rupture of the bladder is usually due to disease of the bladder wall or obstruction at the bladder neck with gross overdistention. Paralytic lesions form a small percentage of the cases. Intraperitoneal rupture is more often noted with a diseased bladder wall. The precipitating factor is invariably a sudden increase in intra-abdominal pressure such as attempted micturition, straining at stool, sudden lifting, or forceful attempts to expel a retained placenta.

The author reports a case occurring on the fifth day post partum. The patient had postpartum retention and the rupture was precipitated by turning over on her abdomen as instructed by a midwife. She experienced severe abdominal pain, vomited, and collapsed. Examination revealed rebound tenderness, a lower abdominal mass (puerperal uterus), and the presence of acites with a fluid wave. The provisional diagnosis was a ruptured ovarian cyst. On exploration of the abdomen 3,400 ml. of yellow fluid were removed from the peritoneal cavity. In the fundus of the bladder was a rent admitting two fingers. The necrotic edges were trimmed; the wound closed in layers, and a retention catheter placed in the bladder. The patient recovered after a febrile postoperative course.

While a rare occurrence, this complication again emphasizes the importance of palpating the bladder and involuting uterus daily to detect puerperal retention. Early ambulation is probably the best means of insuring that a patient empties the bladder completely.

THOMAS L. BALL

Hampson, Frank: A Case of Leukosis Occurring in the Puerperium and Showing Deposits in the Endometrium, J. Obst. & Gynaec. Brit. Emp. 58: 47, 1951.

This is a clinical and pathological report of a case of leukosis occurring in the immediate postpartum period, showing deposits in the endometrium. The main clinical features of this very acute and rapidly fatal illness were a "spiking type" of fever, ascites, pericarditis, splenomegaly, and generalized enlargement of the lymph nodes. The patient, aged 21 years, a primigravida, had had a normal delivery but succumbed on the twenty-first day of her illness, excellent treatment notwithstanding. Postmortem examination coupled with the histological study of specimens from many organs, including the uterine endometrium, led to the conclusion that this was a case of leukosis of hemocytoblastic origin. Low-power views of the endometrium show "wide-spread infiltration by large cells of primitive type" and in certain areas these infiltrating cells completely replace endometrial tissue. The reasons for arriving at the diagnosis of leukosis of hemocytoblastic type are discussed.

HARVEY B. MATTHEWS

Sterility, Infertility

Seguy, J., and Tchiloyans, Mlle.: Azoospermia and Sterility. A Statistical Study Upon One Hundred Cases, Gynéc. et obst. 49: 260, 1950.

The authors reviewed 2,054 barren couples to obtain 100 cases of azoospermia, an incidence of approximately 5 per cent. They admitted to this study only those cases whose specimens on two occasions, after centrifugation, failed to reveal sperm. The authors found three main categories in which to list their cases: 46 cases of secretory azoospermia, 47 cases of excretory azoospermia, and 17 cases of cryptogenic azoospermia.

Among the subseries of 46 cases of secretory azoospermia were 21 cases exhibiting testicular atrophy, 12 with bilateral cryptorchidism, 2 cases with history of traumatic testicular changes, and 11 cases of bilateral orchitis upon basis of mumps. The authors regard mumps septicemia as one which imparts a seriously unfavorable prognosis. He notes the preventive therapy of using 5.0 mg. of stilbestrol daily for 6 days, in the effort to diminish testicular activity during the mumps episode.

In the second category of excretory azoospermia are two subseries classified as the "curable" and "incurable" groups. Among the former were 25 cases of gonococcal epididymitis, 1 case of *B. coli* epididymitis, and 4 cases exhibiting epididymial cysts. In the latter group, the "incurables," were 5 cases of tubercular epididymitis and 2 cases of secondary stricture of the ductus deferens. In the third major category were 17 cases classed as cryptogenic azoospermia. The cases in this group were so classed because no other demonstrable etiological factor could be ascertained.

In conclusion the authors considered that in only about one-third of their series was a therapeutic trial indicated and the greater majority of these derived from those classified as excretory azoospermic cases.

CLAIR E. FOLSOME

Venereal Diseases

Raskin, Raymond A.: Congenital Syphilis in One of Apparently Identical Twins, Am. J. Syph., Gonor. & Ven. Dis. 35: 334, 1951.

This communication includes a review of the literature and a case report. The occurrence of syphilis in one of a pair of twins was first reported in 1859, and, since that date, there have been about 10 additional reports, the last in 1941. The case detailed

is that of a pair of male twins born shortly after the mother had registered for delivery. Because the mother's STS (serologic test for syphilis) was positive and there had not been time to institute antibiotic therapy during the antenatal course, both infants were referred to the pediatrics service for study. On admission, neither presented clinical evidence of syphilis and they were not treated. The neonatal course was uneventful except that twin A developed a rather marked anemia and was given a blood transfusion. Both infants were discharged from the hospital 6 weeks after birth in good condition. Seventeen days later twin A was brought back to the pediatric clinic with jaundice and an enlarged liver. The STS, the spinal fluid Wassermann, and the colloidal gold test were positive and x-ray examination revealed bony changes characteristic of congenital syphilis. Following the diagnosis of syphilis in twin A, twin B was sent for. Physical examination, blood and spinal fluid Wassermanns, and x-ray of the skeleton showed no sign of syphilis. Twin A was treated with penicillin for 10 days and, in spite of the lack of evidence of syphilis in twin B, it was decided to treat him in a similar manner. After this, both twins were followed and neither showed signs of congenital syphilis. The STS in twin A became negative and the x-rays showed disappearance of the syphilitic changes noted above. In summary, the author notes that, because the placenta was not examined at the time of birth, the diagnosis of identical twins is not irrefutable. At the same time, it was emphasized that the children have developed in a manner supporting the diagnosis of identical twins. In discussing the pathogenesis, the possibility of twin A being infected during the actual delivery is conceded but felt to be remote. Thus, in this case, as in those previously reported, no definite explanation can be offered for the occurrence of congenital syphilis in one of a pair of apparently identical twins.

HERBERT J. SIMON

Item

American Board of Obstetrics and Gynecology

The next scheduled examinations (Part II), oral and pathological, for all candidates will be held at the Drake Hotel, Chicago, Ill., by the entire board from Saturday, June 7, through Friday, June 13, 1952. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates.

Applications for certification are now being received for the 1953 examinations. Application forms and Bulletins are sent upon request made to:

ROBERT L. FAULKNER, M.D., Secretary
American Board of Obstetrics and Gynecology
2105 Adelbert Road
Cleveland 6, Ohio

Correspondence

Clinical and Roentgen Pelvimetry

To the Editor:

In the article by John E. Savage, M.D., entitled ''Clinical and Roentgen Pelvimetry: A Correlation,'' published in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, April, 1951, some observations concerning the relationship of the transverse diameter of the pelvic outlet to the interspinous diameter of the midpelvis are certainly open to question.

I am enclosing a section of Table XV from the article in which Dr. Savage shows that of the 65 cases in which the transverse ischial diameter of the pelvic outlet was under 8.5 cm., only 10 showed a midplane interspinous diameter of 9 cm. or less. Dr. Savage measured the interspinous diameter by x-ray and the transverse ischial diameter by external pelvimetry. In a series of 935 cases in which all diameters were measured by x-ray pelvimetry Mengert[1] showed that the intertuberous diameter was shorter than the interspinous in only two instances, and then the difference was negligible. In other words, the transverse diameter of the midplane is commonly shorter than the transverse diameter of the outlet. There is no congenital anomaly or acquired disease which will narrow the tuberosities of the ischium without also narrowing the lower part of the innominate bones. In other words, there can be no serious outlet contraction without commensurate contraction of the midplane.

TABLE XV. SIXTY-FIVE CASES IN WHICH CLINICAL MEASUREMENT OF TRANSVERSE ISCHIAL DIAMETER OF PELVIC OUTLET WAS 8.5 TO 6.5 CM.

CLINICAL MEASUREMENT OF TRANSV. ISCHIAL DIAMETER OF OUTLET, CM.	8.5	8.5 TO 8.0	8.0 TO 7.5	7.5 TO 7.0	7.0 TO 6.5	TOTAL	PER CENT
Total cases	30	23	9	2	1	65	100
Midplane interspinous diameter 9.0 cm. or less	6	3	0	1	0	10	15.3

It therefore follows that Savage's conclusions which show that clinical contraction of the transverse ischial diameter of the pelvic outlet may point to contraction at the midplane in one out of every 3½ cases is probably incorrect.

If it is still generally acknowledged that in so far as measurements themselves are concerned, the x-ray is more accurate than external pelvimetry, then a midplane contraction would be present in practically every case in which the transverse of the outlet measured 8.5 cm. or less.

I would therefore suggest that the transverse ischial diameter of the outlet which obviously is being measured incorrectly by external pelvimetry, be measured by x-ray pelvimetry by one of the standard techniques such as the Snow technique[2] or the Colcher-Sussman.[3]

ARTHUR WEINBERG, M.D., F.A.C.S.

References

1. Mengert, W. F.: J. A. M. A. 138: 169, 1948.
2. Snow, W.: Clinical Roentgenology of Pregnancy, Springfield, Ill., 1942, Charles C Thomas.
3. Colcher, A. E., and Sussman, W.: AM. J. OBST. & GYNEC. 57: 510, 1949.

FAR ROCKAWAY, N. Y.
NOVEMBER 15, 1951.

Reply by Dr. Savage

To the Editor:

Thank you very much for forwarding Dr. Arthur Weinberg's letter.

In reply, I would like to state that we made no claim for the complete accuracy of clinical pelvimetry; and at the time of the accumulation of the data for this paper, we were not satisfied with the accuracy of any of the existing methods for the roentgen measurement of the transverse ischial diameter. Therefore, we called attention to the relationship of the

clinical measurement of the transverse ischial diameter to that of the roentgen measurement of the midplane interspinous diameter, as found in our data, simply to demonstrate that a clinically contracted outlet should lead one to have roentgen pelvimetry studies made in such cases.

<div align="right">JOHN E. SAVAGE, M.D.</div>

BALTIMORE, MD.
DECEMBER 15, 1951.

Pelvic Inlet Contraction

To the Editor:

In Dr. D. Frank Kaltreider's article on the value of the criteria for inlet contraction published in the September, 1951, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, he reaches the general conclusion that when the five yardsticks, obstetrical conjugate, Mengert's areas, Allen's areas, Weinberg and Scadron's sums, and Moir's graph, were used by other obstetricians (Kaltreider), confidence in them was not justified.

In Kaltreider's evaluation of the various methods his criteria for difficult deliveries are defined as follows: "(1) The biparietal diameter of the fetal head has not passed the inlet after a well-defined trial of labor and cesarean section is done, and (2) vaginal delivery has been accomplished but the babies have had intracranial injury. All cases of elective cesarean section have been omitted as well as all sections for uterine inertia. All other deliveries were considered easy or normal."

In our study,[1,2] difficult deliveries included some vaginal deliveries in which the baby did not suffer a fatal or obvious intracranial hemorrhage. We classified as difficult deliveries the following types of cases which Kaltreider evidently classified as easy and normal:

1. Stillbirth due to asphyxiation from impacted shoulders.
2. Traumatic injury to the baby resulting in facial paralysis and Erb's palsy.
3. Fracture of the cranial bones unassociated with intracranial hemorrhage.
4. Cases with extensive soft tissue damage to the mother such as traumatic separation of the symphysis pubis, vesicovaginal fistula, extensive sulcus and third-degree perineal lacerations.
5. Cases in which the baby suffered a clinical brain injury manifested by shock, fever, cyanosis, failure to nurse, and so forth, but in which intracranial hemorrhage was not proved by autopsy or spinal tap.
6. Those cases in which the results were seemingly good from both the maternal and fetal standpoint but the amount of force used was such that grave anxiety was entertained about the future of the baby. It is realized that in some cases of traumatic brain injury the clinical picture does not develop until after the baby is discharged from the hospital. A long-term follow-up is necessary to determine the incidence of cerebral palsy and chronic subdural hematoma.

When conducting a trial of labor in the face of high-grade disproportion it should be realized that one of the most unfortunate things that may happen to a woman is to develop such a powerful labor that vaginal delivery is made possible with disastrous results to mother and baby.[3]

Moir,[4] Mengert, Moloy, and I do not use the rigid classification of difficult deliveries proposed by Kaltreider, and that may be the reason that our indices work in our hands and not in his.

<div align="right">ARTHUR WEINBERG, M.D.</div>

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2. Weinberg, A., and Scadron, S. J.: AM. J. OBST. & GYNEC. 52: 255, 1946.
3. Moloy, H. C., and Steer, C. M.: AM. J. OBST. & GYNEC. 60: 1135, 1950.
4. Moir, J. Chassar: J. Obst. & Gynaec. Brit. Emp. 54: 20, 1947.

1462 GREENPORT ROAD
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DECEMBER 20, 1951.

Reply by Dr. Kaltreider

To the Editor:

It is gratifying to read Dr. Weinberg's comments on the paper under discussion. His remarks are pertinent, and have made me realize that in my zeal for brevity I have committed errors of omission.

Where he states "by other obstetricians (Kaltreider)," it should have been mentioned that "other obstetricians" refers to twelve (12) physicians on the staff of the University Hospital. I, personally, contributed a very small role.

Anent his six classifications of difficult deliveries in addition to intracranial injury, may I say:

1. In this series we did not encounter asphyxiation from impacted shoulders. Our experience in this field has been limited in the past to multiparity of rather high order or to diabetic patients. Seventy-four per cent of the patients were primigravidas. Many of the pelvimetries in multigravidas were for previous section.

2. Traumatic injury to the baby, excluding facial paralysis, was included. Babies with facial paralysis appeared to have been delivered through contracted midplanes and outlets, since the inlet had been surmounted. We did not feel that difficulty with the midplane alone should be included, if the inlet were surpassed. This was a paper on inlet contraction only. That is why they were considered easy deliveries.

3. There were no fractures of the cranial bones.

4. There were no traumatic separations of the symphysis recognized, nor did any patient exhibit symptoms which would point toward this complication. We have not seen a vesicovaginal fistula following delivery in our patients in over 15 years. Third-degree lacerations may be pertinent to midplane and outlet contractions, but I fail to see their relationship to inlet difficulty.

5. We were liberal in our diagnosis of intracranial hemorrhage. Poor neonatal course of the baby with "twitchings" was sufficient for diagnosis.

6. Since this report was concluded in July, 1950, we could not follow these babies. We cannot therefore take long-term follow-ups into consideration in this study.

Dr. Weinberg's definition of difficult delivery in his comments is enlightening and valuable, since it could not be located in any of his papers.

Dr. Moloy's contribution has not been analyzed by us. We hope to do this in the future.

D. FRANK KALTREIDER, M.D.

UNIVERSITY HOSPITAL
BALTIMORE 1, MD.
DECEMBER 15, 1951.

Acute Renal Failure

To the Editor:

The December number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY contains an article by Drs. Chesley and McCaw describing the biochemical findings in association with acute renal failure, especially in the recovery stage, and attempting correlation of these with basic pathology.

They have, however, overlooked in Sheehan's findings a most vital and significant associated state present in the anuric kidney post mortem, the survival of the juxtamedullary nephron apparatus.

A similar histology was described at least ten years previous to Sheehan by Shaw Dunn and Montgomery, also of the Glasgow School, and an understanding of its importance was missed in the absence of knowledge of the Trueta shunt.

Subsequently Govan and MacGillivray had confirmed these renal postmortem appearances. Special staining by benzidene (Solymoss) and by Pickworth's stains (Lancet, Dec. 15, 1951, page 1,100) has detected the presence of a diversion of the renal blood flow in eclampsia. Experimental proof in animals that this end state is due to the Trueta shunt has been brought forward by Franklin and Sophian (employing stimulation of the renal nerve in rabbits) which produced varying degrees of "nephron nephrosis" and

finally, its end state, cortical necrosis. Further confirmation has been obtained by Hoff, who by stimulation of the cat's brain succeeded in causing "nephron nephrosis," provided the renal nerves were uncut.

Franklin and Sophian's limited experiments with dioxan indicated that even chemical toxins primarily produce the "shunt" by utilizing a nervous pathway, though eventually a direct action on the renal tubule cells was apparent. With sighting shots they found that oestrogen could also provoke a similar diversion of the renal blood flow though progesterone was without effect. These experiments confirm the underlying pathology of anuria and include every known stimulus for its production.

That anuria results as a consequence of an extreme Trueta mechanism finds explanation in the fact that renal ischaemia is to all intents complete in the cortical zone abolishing glomerular filtration through spasm of the proximal vessels, and incidentally producing such marked oxygen want to parts supplied on the efferent side as to result in eventual destruction of the tubule cell. Associated with this cortical change is a varying degree of circulation in the juxtamedullary nephrons. Usually the blood supply is adequate for their survival but in the acute state it is insufficient for glomerular filtration, and anuria is the outcome. The recovery stage must therefore reveal at first the excretory functioning of the juxtamedullary apparatus, and the chemical findings must in consequence be correctly correlated. In view of the essential histological differences of the nephrons in cortex and juxtamedullary areas, and the invoking of their activity under varying physiological conditions, it would be incorrect to assume that they possessed identical excretory functions. It may well be that as recovery proceeds and cortical activity intrudes into the picture the biochemical assays will show a gradual preponderance of cortical function though the initial stage represents juxtamedullary activity alone.

It will be seen, therefore, that Drs. Chesley and McCaw have overlooked an essential. The purpose of this letter is not academic argument. If anuria is a continuing spasm it is sound therapeutics to overcome it. I am convinced that a continuing ischaemic spasm contributes to its continuance (1) by producing renal pressor substances which Franklin and Sophian suspect from their experiments and (2) by a severely altered *milieu intérieur*. The former does respond to conduction anaesthesia (Hingson, Lund, Cleland, Bittrich, Tuohy), the latter to exchange transfusions (Vallery Radot) and to intestinal dialysis practised with such success by Derot and Hamburger. A combination of these two principles is the logical answer to therapeutics.

I should like once again to assert that pre-eclamptic toxaemia is a less-marked state of the Trueta shunt provoked by a uterorenal reflex depending on the tight-shoe analogy of the primigravid uterus.

JOHN SOPHIAN, M.D.

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66 HARLEY STREET
LONDON, ENGLAND
FEBRUARY 1, 1952

Reply by Dr. Chesley

To the Editor:

In answer to Dr. Sophian's letter, we should say that there is no good evidence that the Trueta shunt is ever operative in the human kidney. If it ever were, acute renal failure would seem to be the syndrome in which the shunt should be most likely. Perhaps the best piece of evidence against such a diversion of the renal blood flow in acute renal

failure is the fact that the renal extraction of oxygen is increased rather than decreased. This means that the renal venous blood has not been "arterialized," and therefore has not been shunted through a by-pass (unless the blood flow through the by-pass is so low and so slow that the cells of the juxtamedullary apparatus extract and consume the oxygen; but that would put the interference with blood flow proximal to the Trueta shunt). Other evidences inconsistent with the operation of the shunt are: (1) there is a marked reduction in the total blood flow of the kidney; and (2) the extraction of PAH recovers faster than does the clearance, indicating normal clearance of such blood as does perfuse the kidney.

A frequent precipitant of the syndrome is hemorrhagic shock, but there is no evidence that this induces the shunt. Van Slyke's group, in an experimental study of hemorrhagic shock, found that the extraction of PAH remains normal as the renal blood flow decreases, even to less than 5 per cent of normal. They interpreted this in the only possible way—there is no shunting of the blood from the cortex to the medulla.

As for the assertion that "pre-eclamptic toxaemia is a less marked state of the Trueta shunt," the fact that the clearances and maximal tubular excretory capacities (Tm) for Diodrast and PAH are normal in pre-eclampsia and eclampsia cannot be explained on any basis other than a normal blood flow to the renal cortex. It is generally accepted that these substances are excreted by the proximal convoluted tubules; these tubules are confined to the renal cortex; any shunting of blood from the cortex would necessarily result in reductions in the clearances and Tm values; clearance and Tm measurements from half a dozen different laboratories have shown normal values in eclampsia; therefore, no shunt.

Finally, if one looks through the *American Journal of Physiology* for the past few years, he will find many reports of failure to induce the Trueta shunt in a variety of experimental animals.

LEON C. CHESLEY, PH.D.

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FEBRUARY 9, 1952

Efficiency of Placental Exchange

To the Editor:

There is indeed nothing new under the sun. In a recent communication to the JOURNAL ("The Efficiency of Placental Exchange in the Human Subject at the Time of Delivery as Determined by Radiosodium Tracer Techniques") we described at some length a method for obtaining repeated fetal blood samples from the umbilical cord which had been delivered through a miniature uterine incision prior to the delivery of the baby by cesarean section. We stated that we had not found any reference in the literature to an employment of a similar technique.

However, further reading has disclosed that N. J. Eastman in 1930 (Bull. Johns Hopkins Hosp. 47: 221, 1930) described the delivery and clamping of loops of the umbilical cord for the study of fetal blood gases prior to the delivery of the infant by cesarean section. In 1932, G. Haselhorst and K. Stromberger (Ztschr. f. Geburtsh. u. Gynäk. 102: 16, 1932) described experiments in which they injected materials into the umbilical cord delivered through a miniature cesarean section incision and reposited the cord within the uterine cavity for several minutes prior to the delivery of the infant.

The method we have described, therefore, differs only in detail and does not represent a new concept in the experimental attack on problems of intrauterine physiology.

I. H. KAISER, M.D.
I. M. CUSHNER, M.D.

MINNEAPOLIS, MINN.
FEBRUARY 5, 1952

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President*, Walter T. Dannreuther, New York. *Secretary*, John I. Brewer, 104 South Michigan Ave., Chicago, Ill. Next meeting, Hot Springs, Va., May 12, 13, and 14, 1952.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President*, Leroy A. Calkins, Kansas City, Kan. *Secretary*, William F. Mengert, 2211 Oak Lawn Ave., Dallas 4, Texas. Annual meeting Hot Springs, Va., September 11, 12, and 13, 1952.

Central Association of Obstetricians and Gynecologists. (1929) *President*, John I. Brewer, Chicago, Ill. *Secretary-Treasurer*, Harold L. Gainey, 116 S. Michigan Ave., Chicago 3, Ill. Annual meeting, Memphis, Tenn., Oct. 30-Nov. 1, 1952.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President*, E. D. Colvin, Atlanta, Ga. *Secretary-Treasurer*, John C. Burwell, Jr., 416 Jefferson Bldg., Greensboro, N. C.

A. M. A. Section on Obstetrics and Gynecology. *Chairman*, Arthur B. Hunt, Rochester, Minn. *Secretary*, Bernard J. Hanley, 1930 Wilshire Blvd., Los Angeles, Calif. Annual meeting, Chicago, Ill., June 9-13, 1952.

New York Obstetrical Society. (1863) *President*, Howard C. Taylor, Jr. *Secretary*, Charles M. McLane, 960 Park Ave., New York 28, N. Y. Second Tuesday, from October to May.

Obstetrical Society of Philadelphia. (1868) *President*, J. Marsh Alesbury. *Secretary*, Paul O. Klingensmith, 133 S. 36th St., Philadelphia 4, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President*, M. Edward Davis. *Secretary*, Edwin J. De Costa, 720 S. Michigan Ave., Chicago 3, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President*, Stanley C. Hall. *Secretary*, Leslie Hughes Tisdall, 615 Third St., Brooklyn 15, N. Y. Third Wednesday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn. N. Y.

The Obstetrical and Gynecological Society of Maryland. (1929) *President*, Emil Novak. *Secretary-Treasurer*, W. Drummond Eaton, 11 E. Chase St., Baltimore 2, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. (1876) *President*, Joseph G. Crotty. *Secretary*, Robert R. Pierce, 116 William Howard Taft Road, Cincinnati 19, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President*, J. B. Marshall. *Secretary*, David E. Booker, Louisville, Ky. Meetings fourth Monday of each month from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. President, William Sharkey. *Secretary-Treasurer*, Jack W. Dowsett, 1020 S. W. Taylor St., Portland 5, Ore. Meetings last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President*, Eugene A. Conti. *Secretary-Treasurer*, David Katz, 103 Century Bldg., Pittsburgh 22, Pa. Meetings, first Monday of each month, October to May.

Obstetrical Society of Boston. (1861) *President*, George W. Waterman. *Secretary*, A. Gordon Gauld, 1480 Beacon Street, Brookline 46, Mass. Third Tuesday, October to April, Harvard Club.

New England Obstetrical and Gynecological Society. (1929) *President*, Arthur E. G. Edgelow, Springfield, Mass. *Recorder*, Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President*, Roy E. Fallas, Los Angeles, Calif. *Secretary-Treasurer*, Donald G. Tollefson, 511 South Bonnie Brae St., Los Angeles 5, Calif.

Washington Gynecological Society. (1933) *President*, J. Bay Jacobs. *Secretary*, Allan E. King, 915 19 Street, N.W., Washington, D. C. Fourth Saturday, October, November, January, March, May.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* Harry Meyer. *Secretary,* Abe Golden, 1430 Tulane Ave., New Orleans 12, La. Meetings held October, November, January, March, and May.

St. Louis Gynecological Society. (1924) *President,* Paul Fletcher. *Secretary,* J. Russell Vaughan, 634 North Grand Blvd., St. Louis 3, Mo., Regular meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President,* Donald Dallas. *Secretary,* Donald W. de Carle, 2000 Van Ness Ave., San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* S. Foster Moore. *Secretary-Treasurer,* Carey Hiett, 603 College Avenue, Fort Worth 4, Texas.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President,* O. W. Picard. *Secretary,* Carl F. Shelton, 910 David Broderick Tower, Detroit 26, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Central New York Association of Gynecologists and Obstetricians. (1938) *President,* Nathan N. Cohen. *Secretary,* Merton C. Hatch, Medical Arts Bldg., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. (1940) *President,* W. N. Jones. *Secretary,* Herbert H. Thomas, 1005 South Twenty-first Street, Birmingham, Ala.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President,* Gerald Thomas. *Secretary-Treasurer,* Hugh Nuckols, Seattle, Wash. Meetings held on third Wednesday of each month, Washington Athletic Club.

Denver Gynecological and Obstetrical Society. (1942) *President,* Edward L. Harvey. *Secretary-Treasurer,* Jack M. Simmons, Jr., 804 Republic Bldg., Denver 2, Colo. Meetings held first Monday of every month from October to May (inclusive).

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* Thomas A. Leonard. *Secretary-Treasurer,* Alice D. Watts, 324 East Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President,* Jesse A. Rust, Jr. *Secretary-Treasurer,* Ralph L. Hoffman, 2111 Fifth Ave., San Diego 1, Calif. Meetings held on the last Friday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Robert B. Woodhull, Minot, N. D. *Secretary-Treasurer,* John S. Gillam, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President,* Henry C. Spalding. *Secretary,* Chester D. Bradley, 2914 West Avenue, Newport News, Va. Meetings held in April and October.

Columbus Obstetric-Gynecologic Society. (1944) *President,* Allan C. Barnes. *Secretary,* Leonard B. Greentree, 350 East Broad St., Columbus, Ohio. Meetings held last Wednesday of each month from September to May.

Nassau Obstetrical Society. (1944) *President,* Robert S. Millen. *Secretary-Treasurer,* Peter La Mariana, Williston Park, L. I., N. Y. Meetings, bimonthly from October to May.

Bronx Gynecological and Obstetrical Society. (1924) *President,* Benjamin Karen. *Secretary.* Alex Charlton, 1749 Grand Concourse, New York 53, N. Y. Meetings, fourth Monday monthly from October to May.

Washington State Obstetrical Society. (1936) *President,* E. Gerald Layton. *Secretary-Treasurer,* L. Bruce Donaldson, 805 Medical and Dental Bldg., Seattle 1, Wash. Next meeting to be held Sept. 8, 1951, Washington Athletic Club, Seattle.

Kansas City Gynecological Society. (1922) *President,* Kenneth E. Cox. *Secretary,* James E. Keeler, 4301 Main St., Kansas City, Mo. Meetings last Thursday, September, November, January, and March; first Thursday, May, University Club.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* Gordon Rosenblum. *Secretary-Treasurer,* A. N. Webb, 3130 W. 6th St., Los Angeles 5, Calif.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* F. Bayard Carter. *Secretary,* Richard L. Pearse, 604 W. Chapel Hill St., Durham, N. C. Meetings semiannually.

The Society of Obstetricians and Gynecologists of Canada. (1944) *President,* H. B. Atlee. *Secretary,* K. M. Grant. Annual meeting, June, 1950.

Akron Obstetrical and Gynecological Society. (1946) *President,* Donald C. Snyder. *Secretary-Treasurer,* Robert M. DeWitt. Meetings held third Friday of January, April, July, and October, City Club of Akron, Ohio Bldg.

Minnesota Obstetrical and Gynecological Society. *President,* William F. Mercil. *Secretary-Treasurer,* Rodney F. Sturley, 350 Saint Peter St., St. Paul, Minn. Meetings held spring and fall.

Miami Obstetrical and Gynecological Society. (1946) *President,* John D. Milton. *Secretary,* Richard F. Stover, 701 duPont Bldg., Miami, Fla. Meetings, second Thursday in January, March, May, and November.

Omaha Obstetrical and Gynecological Society. (1947) *President,* Ralph Luikhart. *Secretary-Treasurer,* Donald C. Vroman, 813 Medical Arts Bldg., Omaha 2, Neb. Meetings held third Wednesday in January, March, May, September, November.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* John W. Records. *Secretary-Treasurer,* Henry G. Bennett, Jr., 800 Northeast 13 Street, Oklahoma City 4.

Cleveland Obstetrical and Gynecological Society. (1947) *President,* J. L. Reycraft. *Secretary,* G. Keith Folger, 10515 Carnegie Ave. Meetings on fourth Tuesday of September, November, January, March, and May at University Club, 3813 Euclid Ave., Cleveland 15, Ohio.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* Raymond T. Potter. *Secretary,* Felix H. Vann, 242 Engle St., Englewood, N. J. Meetings semiannually.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* Herbert E. Bowles. *Secretary,* James T. S. Wong, 1415 Kalakaua Ave., Honolulu, T. H. Meetings third Monday of each month, Mabel Smyth Building.

Oregon Society of Obstetricians and Gynecologists. *President,* James M. Whitely. *Secretary-Treasurer,* William O. Thomas, Jr., 1735 N. Wheeler Ave., Portland 12, Ore. Meetings held on third Friday of each month from October to May.

National Federation of Obstetric-Gynecologic Societies. (1945) *President,* Ralph E. Campbell. *Secretary,* Woodard D. Beacham, 429 Hutchinson Memorial Bldg., New Orleans 13, La.

Dayton Obstetrical and Gynecological Society. (1937) *President,* C. E. Mumma. *Secretary,* N. J. Thompson, 610 Harries Bldg., Dayton 2, Ohio. Meetings, third Wednesday monthly from September through June at the Van Cleve Hotel.

Dallas-Fort Worth Obstetric and Gynecologic Society. (1948) *President,* W. P. Devereux. *Secretary,* Oran V. Prejean, 4317 Oak Lawn Ave., Dallas, Texas. Meetings in spring and fall.

Queens Gynecological Society. (1948) *President,* James, V. Rizzi. *Secretary,* George Schaefer, 112-25 Queens Blvd., Forest Hills, N. Y. Meetings held second Wednesday in February, April, October, and December, at the Queens County Medical Society Bldg.

Mississippi Association of Obstetricians and Gynecologists. (1947) *President,* John F. Lucas, Greenwood, Miss. *Secretary-Treasurer,* Claude G. Callender, 727 Carlisle St., Jackson 2, Miss. Meetings held semiannually.

Florida Obstetric and Gynecologic Society. (1948) *President,* Robert G. Spicer. *Secretary-Treasurer,* Dorothy D. Brame, 1235 Kuhl Ave., Orlando, Fla. Next annual meeting, April, 1951, at Hollywood, Fla.

South Carolina Obstetrical and Gynecological Society. (1946) *President,* John M. Fleming. *Secretary-Treasurer,* Frank B. C. Geibel, 1517 Hampton St., Columbia 1, S. C. Meetings held in spring and fall.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* Milton G. Potter. *Secretary,* Harry G. LaForge, 957 Delaware Ave., Buffalo, N. Y. Meetings held on the first Tuesday of October through May at the Saturn Club.

El Paso Gynecological Society. (1948) *President,* C. C. Boehler. *Secretary-Treasurer,* Robert J. Cardwell, 414 Banner Bldg., El Paso, Texas.

Kentucky Obstetrical and Gynecological Society. (1947) *President,* Clyde Sparks, Ashland, Ky. *Secretary-Treasurer,* J. B. Marshall, Louisville, Ky.

Indianapolis Obstetrical and Gynecological Society. (1947) *President,* Gerald W. Gustafson. *Secretary-Treasurer,* C. O. McCormick, Jr., 621 Hume Mansur Bldg., Indianapolis 4, Ind. Meetings held in January, April, and October.

Houston Obstetrical and Gynecological Society. (1939) *President,* E. A. Chandler. *Secretary-Treasurer,* J. T. Armstrong, Hermann Professional Bldg., Houston 5, Texas. Meetings held first Tuesday of each month except July, August, and September.

Iowa Obstetric and Gynecologic Society. *President,* J. H. Randall. *Secretary,* William C. Keettel, Iowa City, Iowa.

Memphis Obstetrical and Gynecological Society. (1950) *President,* Frank E. Whitacre. *Secretary,* William F. Mackey, Memphis, Tenn. Meetings, fourth Friday, October to May.

Birmingham Obstetrical and Gynecological Society. (1949) *President,* W. N. Jones. *Secretary,* Herbert H. Thomas, 1005 South Twenty-First St., Birmingham, Ala. Meetings four times yearly.

Mobile Obstetrical and Gynecological Society. (1949) *President,* G. J. Mitchell. *Secretary,* A. J. Brown, 57 St. Francis St., Mobile, Ala. Meetings held second Thursday of January, April, July, and October.

Utah Obstetrical and Gynecological Society. (1948) *President,* William M. Nebeker. *Secretary,* Vernal H. Johnson, 2279 Jackson Ave., Ogden, Utah. Meetings held second Thursday of October, December, March, and May, at the University Club, Salt Lake City.

Inter-urban Obstetrical and Gynecological Society. (1949) *President,* D. E. Cannell. *Secretary,* E. R. Duggan, 16 North Goodman St., Rochester 7, N. Y. Next meeting will be held in Toronto, October, 1951.

New Mexico Obstetrical and Gynecological Society. (1947) *President,* Louis McRae. *Secretary-Treasurer,* LeRoy J. Bowers, Lovelace Clinic, Ridgecrest Drive and Gibson Ave., Albuquerque, N. Mex. Meetings held third Thursday in March, June, September, and December.

Pacific Northwest Obstetrical and Gynecological Association. (1947) *President,* Frank L. MacPhail. *Secretary,* Richard D. Reekie, W. 407 Riverside Ave., Spokane 8, Wash. Next annual meeting, June 25-28, 1952, Many Glaciers Hotel, Glacier Park, Montana.

Southwest Obstetrical and Gynecological Society. (1951) *President,* Preston T. Brown, Phoenix, Ariz. *Secretary,* Jesse A. Rust, Jr., 3115 University Ave., San Diego, Calif.

Montana Obstetrical and Gynecological Society. (1946) *President,* Earl L. Hall, Great Falls, Mont. *Secretary-Treasurer,* Harold W. Fuller, Great Falls Clinic, Great Falls, Mont. Meetings semiannually. Next meeting, The Diamond Ranchotel, Boulder, Mont., April 19-20, 1952.

Madison Obstetrical and Gynecological Society. (1950) *President,* Jack H. Kamholz. *Secretary,* Jack H. Kamholz, 1901 Monroe St., Madison 5, Wis. Meetings monthly except in July, August, and September.